NLM/TIRC-81/2

THE EFFECTS OF ENVIRONMENTAL CHEMICALS ON THE IMMUNE SYSTEM

A Selected Bibliography with Abstracts 1969-1980

by

S. G. Winslow

Toxicology Information Response Center

Oak Ridge National Laboratory

November 1981

Prepared in cooperation with the

NATIONAL LIBRARY OF MEDICINE

FOR THE

INFORMATION RESPONSE TO CHEMICAL CRISES PROJECT

by the

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY

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CONTENTS

INTRODUCTION

The Effects of Environmental Chemicals on the Immune System contains 216 bibliographic references to the published literature from 1969 to 1980. Each bibliographic listing contains a citation (in alphabetical order by author), an abstract (where available), chemical name(s), and species used. Abstracts were prepared by the Toxicology Information Response Center staff. Several indices (chemical name, species, and title) are provided as aids in accessing this material.

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BIBLIOGRAPHIC REFERENCES

1
Adkinson, N. F., Jr. 1977. **Environmental influences on the immune system and allergic reactions.** *Environmental Health Perspectives* 20:97-103.

Environmental interactions with the immune system may result in two types of adverse outcomes: immunodeficiency or immunopathology. Immunodeficiency most commonly results from ionizing radiation or as a recognized side effect of drug therapy, usually cancer chemotherapy. Although environmentally triggered immunopathology is a source of considerable morbidity and mortality, there is little basis for believing that biologically significant suppression of immune competence in man results from more subtle interactions with environmental agents. Research is needed in these areas: basic mechanisms of immunopathological reaction, development of methods for advance assessment of the potential immunogenicity of new industrial chemicals, development of accurate methods for implicating or excluding immunological factors in the etiology of hypersensitivity, and identification of the risk factors which predispose to immunological outcomes in sensitive individuals.

2
Ado, V. A. 1974. **Suppression of immunity by chemical agents.** *Patologicheskaya Fiziologiya i Eksperimentalnaya Terapiya (U.S.S.R.)* 5:82-87 (RUS).

3
Alekseeva, O. G. 1974. **Main objectives of immunological investigations on problems concerned with industrial hygiene and occupational pathology.** *Gigiena Truda i Professional'nye Zabolevaniya* 2:1-6 (RUS).

Basic problems in the domain of immunological investigations related to industrial hygiene and occupational pathology are discussed. The paper also refers to the problems of general allergology and immunology.

4
Alekseeva, O. G.; Brekhova, N. N.; Vasileva, E. V.; Volkova, A. P.; Grishina, T. I.; Ermakova, N. G.; Karpenko, O. V.; Bobrishchev-Pushkin, D. M.; Nikitina, L. S. 1979. **Use of immunological research methods in the clinical-hygienic verification of the maximum permissible concentration of industrial allergens.** *Gigiena Truda i Professional'nye Zabolevaniya* 9:9-15 (RUS).

Autoimmunity, nonspecific resistance of the body to infection, and size and functional state of various lymphocyte populations were determined in workers having occupational contact with beryllium. Comprehensive immunological examinations permit a complete characterization of the biological effect of an industrial allergen in the absence of clinically manifested responses of occupational disorders. The maximum permissible concentration of beryllium cannot be considered as safe as far as the development of allergic disorders is concerned.

Beryllium

HUMAN STUDIES

5
Alekseeva, O. G.; Vasileva, E. V.; Orlova, A. A. 1974. **Abolition of natural tolerance and the influence of the chemical allergen beryllium on autoimmune processes.** *Bulletin of the World Health Organization* 51(1):51-58.

Six beryllium-containing autoantigens were identified in lung nucleoproteins accompanying a partial loss of normal tissue and serum antigens. Antibodies to the new antigens and, in smaller amounts, to normal lung tissue were found in the sera of rats with experimental berylliosis, as well as in patients. Patients with granulomatous berylliosis had antibodies to DNA, RNA, and extracts of normal homologous heart, spleen, liver, and thyroid in quantities that correlated with the clinical picture and with the effectiveness of glucocorticoid therapy. Interruption of natural tolerance in all cases and the development of autoimmune granulomatous berylliosis in some patients led to the assumption that the mechanism was effective under the influence of additional endogenous factors; diseases producing an accumulation of autoantibodies could provide the stimulus for the appearance of these factors.

Beryllium

HUMAN STUDIES; RATS

6
Alekseeva, O. G.; Vasileva, E. V.; Orlova, A. A. 1975. **Interruption of natural tolerance and effect of the chemical allergen beryllium on autoimmune processes.** *Byulleten Vsemirn. Organiz. Zdravookhranenie* 51(1):48-54 (RUS).

Beryllium

7
Allen, J. R.; Lambrecht, L. 1978. **Responses of rhesus monkeys to polybrominated biphenyls.** *Toxicology and Applied Pharmacology* 45(1):340-341.

Rhesus monkeys were fed diets containing 0.3, 1.5, and 25.0 ppm of a commercial mixture of polybrominated biphenyls (PBB). Seven adult females have been on the 0.3 ppm of PBB for approximately one year and have consumed about 25 mg of the PBB mixture. In addition to a loss of weight, the monkeys experienced changes in the levels of serum estradiol and progesterone during the initial 6 months of exposure which could be correlated with altered menstrual cycles. After six months of exposure the animals were bred, and all conceived after one to four breedings. Two of the seven animals aborted, and the remaining five had term infants. Animals consuming 1.5 ppm of PBB experienced a moderate weight loss and periorbital edema. The third group, which received 25 ppm of PBB in the diet for ten weeks, experienced a weight loss, abdominal distension, and diarrhea. The latter two groups show alterations in B- and T-cell function. Relatively low levels of PBB exposure may affect reproduction, weight gain, and immunologic competence of rhesus monkeys.

Polybromobiphenyl compounds

MONKEYS

8
Allen, J. R.; VanMiller, J. P. 1977. **Health implications of 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure in primates.** *Pentachlorophenol*, ed. K. R. Rao, pp. 371-379. New York: Plenum Press.

Effects of tetrachlorodibenzo-p-dioxin (TCDD) on human health are reviewed. Accidental exposures have afforded an insight into the consequences of exposure to this substance for humans. The largest exposure accident occurred in north Italy where a mixture of materials containing TCDD exploded over a large area of land being used for industrial, urban, and agricultural purposes. A feature common to all the industrial accidents has been the persistence of TCDD in contaminated areas, as well as the persistence of the toxic effects experienced by those exposed. The long term effects of TCDD exposure are not certain at this time. Results of laboratory investigations on TCDD-exposed nonhuman primates and of low-level exposure of rats to TCDD

are reported. Data thus far indicate that anemia, leukopenia, gastritis, ulceration, reproductive effects, alterations in the immune response, and cancer may be aftermaths of chronic low-level exposure to TCDD.

TCDD, 2,3,7,8-

9
Allison, A. C. 1975. **Effects of silica, asbestos and other pollutants on macrophages.** *Air Pollut. Lung, Proc. Annu. "OHOLO" Biol. Conf., 20th,* ed. E. F. Aharonson, F. Ephraim, A. Ben-David, and M. A. Klingberg, pp. 114-134. New York: Wiley.

A review of the effects of silica, asbestos and other pollutants on alveolar macrophages is presented.

Asbestos; Silica

10
Aripdzhanov, T. M. 1973. **Effect of the pesticides Anthio and Milbex on the immunological reactivity and certain autoimmune processes of the body.** *Gigiena i Sanitariya* (7):39-42 (RUS).

Long-term poisoning of animals with anthio and milbex caused a decrease in the immunological reactivity of the body as revealed by the inhibition of the phagocytic activity, the development of certain autoimmune processes of the blood, and the increase of the agglutinin titer.

Anthio; Phosphorodithioic acid, S-(2-(formylmethylamino)-2-oxoethyl) O,O-dimethyl ester; Milbex; Benzenemethanol, 4-chloro-alpha-(4-chlorophenyl)-alpha-methyl-, mixture with ((4-chlorophenyl)thio)(2,4,5-trichlorophenyl)diazene

11
Askari, E. M.; Gabliks, J. 1973. **DDT and immunological responses. II. Altered histamine levels and anaphylactic shock in guinea pigs.** *Archives of Environmental Health* 26(6):309-319.

Intraperitoneal injection of guinea pigs previously immunized to diphtheria toxoid with 25 mg/kg of DDT prior to challenge with a second dose of diphtheria toxoid resulted in a decrease in lung histamine concentration to 71% of that in controls not receiving DDT. In nonimmunized animals, DDT reduced lung histamine to 62% of that in untreated controls. The number of mast cells was reduced, respectively, to 36% and 67% of that of controls. DDT injection caused release of histamine from mast cells and reduced anaphylactic shock after challenge with diphtheria toxoid.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

GUINEA PIGS

12
Astolfi, E.; Almeida, W. F.; Maccagno, A.; Gaeta, R. 1979. **Immunotoxicological study of pesticides.** *Developments in Toxicology and Environmental Science* 4:471-473 (SPA).

Immunotoxicological tests were performed on 41 factory workers exposed to DDT and 11 unexposed controls. The tests for rheumatoid factors, antimitochondrial antibodies, anti-alpha-fetoprotein antibodies, and glomerular basal anti-membrane antibodies were negative in both groups. The antinuclear antibody test was positive in one control subject. Tests for antibodies to smooth muscles were positive in 5 of 41 and 2 of 11 cases, respectively. Tests for antibodies to striated muscles were positive in 13 of 41 and 5 of 11 cases. The differences in these tests were not significant statistically. The test for antibody to gastric parietal cells was positive in 5 of 41 and 0 of 11 cases, respectively. The findings indicate that DDT does not produce autoantibodies. The negative anti-alpha-fetoprotein antibody tests suggest that DDT does not have hepatic neoplasiogenic effects.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

HUMAN STUDIES

13
Atabaev, S. T.; Boiko, I. B.; Ilina, V. A. 1978. **Effect of pesticides on the immunological state of the body.** *Gigiena i Sanitariya* (8):7-10 (RUS).

Immunological responses of farm workers in the Syrdar'insk region were measured prior to cultivation and after pesticide use. In tests using basudin, polychloropinene, and calcium cyanamide, disturbances of immune reactions were most pronounced with organochlorine pesticides due to their accumulation. Depression of immune reaction appears during the latent period of intoxication and may serve as an early sign for preventative measures. In a rat assay, dose-dependent changes in antibody titers were noted at 1/20, 1/100, and 1/1000 LD50.

Basudin; Phosphorothioic acid, O,O-diethyl O-(6-methyl-2-(1-methylethyl)-4-pyrimidinyl) ester; Polychloropinene; Calcium cyanamide; Cyanamide, calcium salt (1:1)

HUMAN STUDIES; RATS

14
Atwal, O. S.; Samagh, B. S.; Bhatnagar, M. K. 1975. **A possible autoimmune parathyroiditis following ozone inhalation: II. A histopathologic, ultrastructural, and immunofluorescent study.** *American Journal of Pathology* 80(1):53-68.

Parathyroid glands of rabbits were studied and histologic, ultrastructural, and immunofluorescent changes noted after 48 hr of ozone inhalation at a dosage of 0.75 parts per million. Among the changes observed were hyperplastic parathyroiditis followed by capillary proliferation and leukocytic infiltration. The ultrastructural changes included degeneration of nuclei, atrophy of the mitochondria, dilatation and atrophy of the endoplasmic reticulum of the chief cells of the parathyroid gland, proliferation of the venous limb of the capillary network, and the prominent interstitial elements. Immunofluorescent techniques revealed positive immunologic response. Ozone inhalation may trigger an immune reaction which causes inflammatory injury to the parathyroid gland. The possibility that the modified functional chemical groups of the parathyroid gland act as autoantigens is discussed.

Ozone

RABBITS

15
Barlogova, S.; Ulrich, L. 1977. **Some immunological findings in silicosis.** *Journal of Hygiene Epidemiology Microbiology and Immunology (Prague)* 21(3):247-253.

Results of an experimental study of the effect of quartz administered intratracheally to the immune status of Wistar rats are described. Data obtained showed that a significant inhibition of antibody formation to human albumin took place in animals with experimental silicosis in comparison with control rats.

Enhancement of the intensity of the delayed-type hypersensitivity to tuberculin was also noted.

Silica

RATS

16
Barnes, D. W.; Munson, A. E. 1978. **Cadmium-induced suppression of cellular immunity in mice.** *Toxicology and Applied Pharmacology* 45(1):350.

Groups of male and female ICR adult mice were orally gavaged with single, daily doses of 0.65, 32.6, or 65.2 mg/kg of cadmium chloride for 14 or 90 days. The effect of cadmium on delayed type hypersensitivity (DTH) was determined by footpad swelling in response to sheep erythrocytes (SRBC). After 14 days, the highest cadmium dose significantly suppressed footpad swelling in both male and female mice. In female mice footpad swelling also decreased after the lower doses. After 90 days of treatment, the DTH response to SRBC decreased only at the high dose in males. In female mice suppression of DTH was significantly greater than in males and was dose-dependent, with almost total suppression at the highest dose. The functional activity of the mononuclear phagocytic system (MPS) was measured by blood clearance and organ distribution of 125I-labeled Listeria monocytogenes. MPS activity also decreased after 90 days of treatment as evidenced by significant reduction in uptake of Listeria into livers of both female and male mice treated with the two highest doses.

Cadmium

MICE

17
Bekesi, J. G.; Roboz, J.; Anderson, H. A.; Roboz, J. P.; Fischbein, A. S.; Selikoff, I. J.; Holland, J. F. 1979. **Impaired immune function and identification of polybrominated biphenyls (PBB) in blood compartments of exposed Michigan dairy farmers and chemical workers.** *Drug and Chemical Toxicology* 2(1/2):179-191.

Results of studies on the impact of PBBs in exposed Michigan farm residents are presented. Compared to controls, farm residents exposed to PBBs showed an increased sensitivity to recall antigens as measured in vivo by delayed cutaneous hypersensitivity response. In addition, 17 of 45 examined Michigan farm workers showed significant deviations from the normal range in both percent and absolute number of T-cells. An increased number of lymphocytes without detectable membrane markers, "null cells", were noted in peripheral blood lymphocytes of these people. Significantly reduced cell-mediated response was noted in 18 of the 55 studied workers.

Polybromobiphenyl compounds

HUMAN STUDIES

18
Bellanti, J. A. 1974. **Immunologic responses to chemical pollutants.** *Pediatrics* 53(5 pt. 2):818-819.

19
Belomyttseva, L. A.; Krotkova, S. V.; Sofina, L. I. 1976. **Some immunological indexes of workers in the petrochemical industries suffering from chronic nonspecific lung diseases.** *Aktual'nye Voprosy Okhrana Trudov Khimicheskogo Promyshlennosti,* ed. V. I. Talapin, pp. 109-111 (RUS). Beloruss. Nauchno-Issled. Sanit.-Gig. Inst.: Minsk, USSR.

Workers in a factory manufacturing divinyl-alpha-methylstyrene rubber and synthetic ethanol showed an elevated frequency of chronic bronchitis with bronchiospastic syndrome, frequently complicated by chronic nonspecific pneumonia. An increase of serum gamma-globulins was found in 28% of the patients, and of alpha-1- and alpha-2-globulins in 20%, whereas 12.4% showed a decrease of albumins. Patients with a pronounced asthmoid component showed an elevated titer of pulmonary antibodies and decreased phagocytic activity, whereas simple bronchitis patients showed a high phagocytic index and number.

Divinyl-alpha-methylstyrene; Ethanol

HUMAN STUDIES

20
Bice, D. E. **FBC-Influence of inhaled effluents on pulmonary defense mechanisms.** Research at Lovelace Center for the Health Sciences, Inhalation Toxicology Research Institute, Albuquerque NM; Sponsored by DOE, Germantown MD, code 002674; EY-76-C-04-1-1013; 0/78-N/A.

The use of fluidized bed conversion (FBC) as a major energy source may result in the production of effluent materials which, if inhaled, might cause adverse health effects. The products of primary concern are trace metals, hydrocarbons, and other pollutants associated with fine particle emissions. The degree to which these materials may pose a health hazard depends upon the functional integrity of various pulmonary defense mechanisms. Notable among these are immunologic responses, macrophage responses, mucocilliary clearance, and nonspecific antimicrobial defenses. To assess the effects of FBC effluent products on immunologic function, rodents and dogs will be exposed to selected materials by inhalation and instillation, and, at various times following exposure, the response to instilled or aerosolized antigen determined in lung, lung-associated lymph nodes, spleen, and blood. The additive effects of inhaled pollutants on antimicrobial defenses in compromised animals will be evaluated. Finally, the effects of inhaled FBC effluent materials on mucocilliary clearance will be assessed through the conduct of retention studies at various times after inhalation exposure. These data will assist in predicting human health hazards that might be associated with FBC technology.

DOGS

21
Bice, D. E.; Harris, D. L.; Brooks, A. L.; Mewhinney, J. A. 1980. **The effects of inhaled toxic particles on immune responses following lung immunization.** *Federation Proceedings* 39(3, pt 1):623.

Lung-associated lymph nodes (LALN) are one route of clearance of insoluble particles deposited deep in the lung. To investigate the effects of inhaled particles on immunity in LALN, an initial site of immunity in the lung, Chinese hamsters were exposed to a polydisperse aerosol of plutonium oxide (239PuO2). The mean lung burden was estimated to be 10 nCi eight days following exposure. Control and experimental animals were immunized with sheep red blood cells administered intratracheally, and the number of antibody-forming cells (AFC) in LALN, spleen, and cervical lymph nodes were evaluated six days later. The number of AFC were significantly lower in those animals exposed to plutonium. These results indicate that although plutonium oxide exposure suppressed immune responses in the LALN, their filtering capacity was unaffected and antigen deposited in the lung did not translocate to the spleen. It was concluded that LALN immune function was suppressed and their immune function was not replaced by distant lymphoid tissue.

Plutonium oxide

ANTIBODY RESPONSE

22
Bice, D. E.; Harris, D. L.; Schnizlein, C. T.; Manderly, J. L. 1979. **Methods to evaluate the effects of toxic materials deposited in the lung on immunity in lung-associated lymph nodes.** *Drug and Chemical Toxicology* 2(1/2):35-47.

Methods used to determine if toxic materials deposited in the lung alter immunologic responses following lung immunization are presented. Intratracheal instillation of sheep red blood cells (SRBC) induced a primary immune response in lung-associated lymph nodes of Chinese hamsters and Fischer-344 rats. Few or no anti-SRBC antibody-forming cells (AFC) were found in the spleen or cervical lymph nodes after intratracheal immunization. The number of AFC was significantly suppressed in the lung-associated lymph nodes from hamsters exposed by inhalation of plutonium oxide and in rats exposed by intratracheal instillation of benzo(a)pyrene (BaP). Although the immunologic function of the lung-associated lymph nodes was suppressed by plutonium oxide and BaP exposure, there was no observable increase in the number of AFC in distant lymphoid tissues. Damage to lung cells and/or cells in lung-associated lymph nodes can suppress immunity induced by deposition of antigen in the lung. Even though lung-associated lymph nodes in exposed animals contained lower numbers of AFC, antigen instilled into the lungs of exposed animals did not significantly translocate to distant lymphoid tissues, indicating that the antigen filtering capacity of the lung-associated lymph nodes was not altered.

Plutonium oxide; Benzo(a)pyrene

RATS

23
Blakley, B. R.; Sisodia, C. S.; Mukkur, T. K. 1980. **The effect of methylmercury, tetraethyl lead, and sodium arsenite on the humoral immune response in mice.** *Toxicology and Applied Pharmacology* 52(2):245-254.

Male mice were exposed to methylmercuric chloride, tetraethyl lead, or sodium arsenite for three weeks in the drinking water at various concentrations. The humoral component of the immune system was evaluated using hemagglutination, radial immunodiffusion, and the Cunningham plaque assay (both primary and secondary immune response). Each evaluation of the immune response demonstrated immunosuppressive effects at low metal concentrations. A maximum effect was produced in most instances at a metal concentration of less than 2.0 ppm. Metal concentrations in the liver and kidney showed that a dose-effect relation existed at all metal exposure levels; however, the maximal immunosuppressive effect was observed in spite of increasing tissue concentration of the metal.

Methylmercury; Tetraethyl lead; Sodium arsenite; Chloromethylmercury

MICE

24
Bobrzecka, K.; Konieczny, L.; Pryjma, J.; Ptak, W.; Rybarska, J. 1977. **The immunopotentiating effect of thiosulfate in vivo.** *Experientia (Basel)* 33(12):1654-1656.

The adjuvanticity of Na2S2O3 was examined in mice. Serum IgG, IgM, and transferrin were increased in Balb/c mice given 0.3 mg/g body weight. IgG subclass analyses suggest that this stimulation is nonspecific. Thymocyte-dependent antibody formation was increased about two-fold by thiosulfate, whereas the T-independent response was suppressed slightly.

Sodium thiosulfate

MICE

25
Bozelka, B. E.; Burkholder, P. M.; Chang, L. W. 1977. **Cadmium-induced immunosuppression and splenomegaly in mice.** *American Journal of Pathology* 86(2):21a-22a.

Cadmium

MICE

26
Bozelka, B. E.; Burkholder, P. M.; Chang, L. W. 1978. **Cadmium, a metallic inhibitor of antibody-mediated immunity in mice.** *Environmental Research* 17(3):390-402.

Chronic administration of cadmium chloride to B10-A-2R mice was found to delay onset of appearance and severely depress numbers of splenic IgG and IgM plaque-forming cells (PFC) following injection of sheep erythrocytes. No increase in IgM PFC and only a minimal increase in IgG PFC was noted after a recovery period of at least one month following cessation of cadmium chloride administration. An apparent cadmium-induced splenomegaly was also noted in the intoxicated mice. Immune adherence, rosetting techniques, and immunofluorescence were used to study the cellular morphology of these spleens. It was indicated that the cell type most responsible for the increased spleen size had Fe and complement receptors as well as surface or cytoplasmic immunoglobulins. Populations of polymorphs and macrophages did not contribute significantly to the hyperplasia observed.

Cadmium chloride

MICE

27
Brody, J. E. 1977. **Immunological effects found in people in Michigan who ate food contaminated by PBB.** *New York Times,* 2 August 1977, p. 13.

Serious defects in the immunological cells of Michigan residents who ate food contaminated with a fire retardant containing polybrominated biphenyl (PBBs) were noted. The retardant was accidentally substituted in dairy cattle feed prepared in 1973 by the Michigan Farm Bureau.

Polybromobiphenyl compounds

HUMAN STUDIES

28
Burkle, P. A.; Tonnesmann, E.; Ahnefeld, S.; Nobbe, F.; Federlin, K. 1976. **Experiences with DNCB sensitization in normal human individuals of various age groups.** *Zeitschrift fuer Immunitaetsforschung* 151(2):153-165.

Using dinitrochlorobenzene, the primary cellular immune response of 40 normal individuals was investigated. The response to DNCB in the younger age group was stronger than in the older age group, suggesting a decrease of T (thymus-derived)-cell function in elderly subjects. Due to the potent immunogenicity of this substance and the possibility of cross reactions with numerous similar antigens widely used in the chemical and related industries, this test should only be applied in selected cases.

Dinitrochlorobenzene

HUMAN STUDIES

29
Butcher, B. T.; Jones, R. N.; ONeil, C. E.; Glindmeyer, H. W.; Diem, J. E.; Dharmarajan, V.; Weill, H.; Salvaggio, J. E. 1977. **Longitudinal study of workers employed in the manufacture of toluene diisocyanate.** *American Review of Respiratory Disease* 116(3):411-422.

Workers at a toluene diisocyanate manufacturing plant were studied to determine the effects of the chemical on their health. Studies included health questionnaires, pulmonary function, environmental monitoring, and immunologic testing. Monitoring showed frequent levels of toluene diisocyanate above the threshold limit value. Poor correlation between area and personal exposure levels existed. Development of a positive skin test to a toluene diisocyanate-human serum albumin conjugate by some persons and an increasing incidence of toluene diisocyanate-specific IgE antibodies were noted. Toluene diisocyanate did not induce histamine release from leukocytes in vitro. Most of the clinically sensitive persons demonstrated adverse bronchial response when challenged by inhalation of toluene diisocyanate, and this response was dose-dependent in some.

Toluene diisocyanate; Benzene, 1,3-diisocyanatomethyl-

HUMAN STUDIES

30
Calabrese, A.; Greig, R. A.; Thurberg, F. P.; Robohm, R. A.; Gould, E.; Newman, M. W. 1974. **Physiological response of the cunner, Tautogolabrus adspersus, to cadmium.** *NOAA (National Oceanic and Atmospheric Administration) Technical Report NMFS (National Marine Fisheries Service) SSRF (Special Scientific Report Fisheries)* NMFS SSRF-681, 37 pp. Washington: National Oceanic and Atmospheric Administration.

Changes in enzyme patterns, the induction of histopathological abnormalities, and alterations in the immune response to various antigens were studied in the cunner (Tautogolabrus adspersus).

Cadmium

FISH

31
Carlson, J. E.; Villaveces, J. W. 1977. **Hypersensitivity pneumonitis due to pyrethrum. Report of a case.** *Journal of the American Medical Association* 237(16):1718-1719.

A case of hypersensitive pneumonitis following repeated exposure to a pyrethrum-based insecticide is reported. Following avoidance of the insecticide, the patient's symptoms resolved. This case study adds pyrethrum to the long list of chemicals capable of causing hypersensitivity pneumonitis.

Pyrethrins

HUMAN STUDIES

32
Carter, J. W. 1979. **The effects of polychlorinated biphenyls on T-cell-mediated immunity in mice.** *Anatomical Record, The* 193(3):501.

Polychlorobiphenyl compounds

MICE

33
Ceglowski, W. S.; Ercegrovich, C. D.; Pearson, N. S. 1979. **Effects of pesticides on the reticuloendothelial system.** *Advances in Experimental Medicine and Biology* 121(A):569-576.

Pesticides

34
Chetty, K. N.; Rao, D. S. V. S.; Drummond, L.; Desaiah, D. 1979. **Cobalt-induced changes in immune response and adenosine triphosphatase activities in rats.** *Journal of Environmental Science and Health. Part B. Pesticides, Food Contaminants, and Agricultural Wastes* B14(5):525-544.

Data on biochemical and immunological effects of cobaltous chloride in rats receiving iron-sufficient and -deficient diets are presented. At greater than or equal to 100 ppm cobalt rats showed a significant decrease in thymus and body weights along with a marked reduction in sheep agglutinins, plaque-forming cells, hemoglobin, and hematocrit. Effects were more pronounced in those animals on the iron-deficient diets. Significant decreases in Na^+-K^+ and mitochondrial (oligomycin sensitive) Mg^{2+} ATPase activities were noted in brain and liver tissues of rats maintained on the iron-deficient diets.

Cobalt chloride

RATS

35
Cheville, N. F. 1979. **Environmental factors affecting the immune response of birds. A review.** *Avian Diseases* 23(2):308-314; Western Poultry Disease Conference 27th, Proceedings, pp. 7-9. University of California, Davis CA.

BIRDS

36
Colten, H. R.; Borsos, T. 1974. **Biosynthesis of the second and fourth components of complement. Inhibition in vitro by chemical carcinogens.** *Journal of Immunology* 112(3):1107-1114.

Out of several aromatic amine, azo dye, nitrosamine, and lactone carcinogens and noncarcinogenic analogs tested for inhibition of the biosynthesis of the second (C2) and fourth (C4) components of complement in vitro in guinea pig peritoneal exudate cells, 4-nitroquinoline N-oxide, effective at 10(-7)M, was the most potent. Beta-propiolactone, nitrosomethylurethan, and diphenylnitrosamine also inhibited C2 and C4 synthesis, but their noncarcinogenic analogs had no effect. Some carcinogens may interfere with at least one normal function of the immune system.

Diphenylnitrosamine; Nitrosomethylurethane; Methylnitroso carbamic acid ethyl ester; 4-Nitroquinoline N-oxide; 4-Nitroquinoline-1-oxide; Beta-propiolactone; Oxetanone, 2-; N-Nitroso-N-phenylbenzenamine

GUINEA PIGS

37
Cook, H.; Helland, D. R.; Vanderweele, B. H.; Dejong, R. J. 1978. **Histotoxic effects of polybrominated biphenyls in Michigan dairy cattle.** *Environmental Research* 15(1):82-89.

Tissues from cattle of five herds affected by PBBs in central Michigan were collected on two dates. Results showed lymphocyte infiltration into liver, kidney, small intestine, and lungs. Histology of spleen and lymph nodes and the maintenance

of thymus size indicated high immunological activity, and the susceptibility of the cattle to infections suggested impairment of immunological mechanisms.

Polybromobiphenyl compounds

CATTLE

38
Dandliker, W. B.; Hicks, A. N.; Levison, S. A.; Stewart, K.; Brawn, R. J. 1979. **Effects of pesticides on the immune response.** *U.S. NTIS Report* PB80-130834, 52 pp.; Environmental Science and Technology 14(2):204-210.

Aroclor 1260, Dinoseb, Parathion, pentachloronitrobenzene, piperonyl butoxide, mixed pyrethrins, and Resmethrin were administered intragastrically in corn oil in one dose (one half of LD50) before primary immunization. Cellular immune response was quantified by redness and swelling, histological examination, and by differential temperature measurements of the footpads after antigen challenge. The concentration, binding affinity, and heterogeneity of the serum antibody were determined by fluoroscence polarization measurements. Dinoseb and Parathion depress both the humoral and cellular response. Methotrexate and pentachloronitrobenzene give a late stimulation, while Resmethrin gives an early, sometimes very marked stimulation of the cellular immune response. Other pesticides showed little or no effect under the conditions tested. Effects on the humoral response were limited to changes in antibody concentration, the binding affinity being nearly constant in all instances.

Polychlorobiphenyl compounds; Dinoseb; Phenol, 2-(1-methylpropyl)-4,6-dinitro-; Parathion; Phosphorothioic acid, O,O-diethyl O-(4-nitrophenyl) ester; Methotrexate; L-Glutamic acid, N-(4-(((2,4-diamino-6-pteridinyl)methyl)methylamino)benzoyl)-; Pentachloronitrobenzene; Benzene, pentachloronitro-; Piperonyl butoxide; 1,3-Benzodioxole, 5-((2-(2-butoxyethoxy)ethoxy)methyl)-6-propyl-; Pyrethrins; Resmethrin; Cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-, (5-(phenylmethyl)-3-furanyl)methyl ester

39
Desi, I.; Varga, L.; Farkas, I. 1978. **Studies on the immunosuppressive effect of organochlorine and organophosphoric pesticides in subacute experiments.** *Journal of Hygiene Epidemiology Microbiology and Immunology (Prague)* 22(1):115-122.

Lindane, malathion, and dichlorphos administered orally to male rabbits caused a dose-dependent decrease in Salmonella typhi-induced immune response in the animals, as reflected by blood antibody titers. Animals treated with these pesticides also showed decreased cholinesterase activity in the brain and liver in a dose-related manner, indicating a positive correlation with immunological findings.

Dichlorophos; Phosphoric acid, 2,2-dichloroethenyl dimethyl ester; Lindane; Cyclohexane, 1,2,3,4,5,6-hexachloro-, (1alpha,2alpha,3beta,4alpha,5alpha,6beta)-; Malathion; Butanedioic acid, ((dimethoxyphosphinothioyl)thio)-, diethyl ester

RABBITS

40
DeWeck, A. L. 1977. **Immune responses to environmental antigens which act on skin.** *Federation Proceedings* 36(5):1742-1747.

The skin represents the first line of defense against our environment. Thus it is not surprising that most of the manifestations of an immune response to environmental agents involve the skin at some time. Immunological reactions in the skin may take several forms, indicative of different immunological mechanisms. Contact dermatitis is a prime example of delayed-type sensitivity reactions in the skin. Environmental agents responsible for skin manifestations of delayed-type hypersensitivity are briefly discussed, as are other topics pertinent to the development and manifestations of delayed-type hypersensitivity in the skin.

41
DiCarlo, F. J.; Seifter, J.; DeCarlo, V. J. 1978. **Assessment of the hazards of polybrominated biphenyls.** *Environmental Health Perspectives* 23:351.

International attention was drawn to PBBs by the state-supervised killing of over 35,000 cattle which had been contaminated with PBBs mixed accidentally with animal feed preparations. Despite a low acute toxicity, low doses of PBBs exert a broad range of toxicological, pharmacological, and biochemical effects. In rodents, PBBs are teratogenic, immunosuppressive, and potentially carcinogenic. In bovine, avian, and rodent species, PBBs reduce feed intake and induce mixed-function oxidases of liver microsomes. Effects of these chemicals on humans are controversial, but data indicating immunological, skin, and liver disorders are accumulating. These compounds can enter the fetus by crossing the placental barrier and can be transferred to newborns through breast milk.

Polybromobiphenyl compounds

42
Dinoeva, S. K. 1974. **Dynamics of changes in the immune structure of lymphatic follicles of the spleen during pesticide poisoning.** *Gigiena i Sanitariya* (3):85-87 (RUS).

When administered orally to rats for six months, zineb, (12.5 or 125 mg/kg/day), Sevin (1.5 mg/kg/day), afalon (8 mg/kg/day), or tribufon (5 mg/kg/day) significantly decreased the size of the lymphatic follicles in the spleen. Tribufon had the least pronounced effect.

Afalon; Urea, N'-(3,4-dichlorophenyl)-N-methoxy-N-methyl-; Carbaryl; 1-Naphthalenol, methylcarbamate; Tribufon; Butanoic acid, 2,2,2-trichloro-1-(dimethoxyphosphinyl)ethyl ester; Zineb; Zinc, ((1,2-ethanediylbis(carbamodithioato))(2-))-

RATS

43
Dueva, L. A. 1978. **Immunological manifestations of delayed-type hypersensitivity and problems of specific immunodiagnosis in occupational allergy of chemical etiology.** *Gigiena Truda i Professional'nye Zabolevaniya* 1:19-23 (RUS).

Materials derived from a dynamic clinico-immunological examination of 225 patients with occupational allergoses and allergodermatoses of chemical etiology and also of 300 practically healthy workers exposed occupationally to a number of chemical allergens are presented. Application of various serological and cellular reactions with chemical allergens confirms the pathogenetic role of humoral factors of sensitization in the development of occupational allergic affections of chemical etiology. Immunological methods for specific diagnosis of occupational allergoses are recommended.

HUMAN STUDIES

44
Ehrlich, R.; Silverstein, E.; Maigetter, R.; Fenters, J. D.; Gardner, D. 1975. **Immunologic response in vaccinated mice during long-term exposure to nitrogen dioxide.** *Environmental Research* 10(2):217-223.

The effect of long-term exposure to low concentrations of nitrogen dioxide on the immunological response of mice vaccinated with a purified influenza virus vaccine is examined. Parameters examined include hemagglutination-inhibition, serum neutralization, antibody formation, and serum immunoglobulin levels.

Nitrogen oxide

MICE

45
Ercegovich, C. D. 1973. **Relation of pesticides to immune responses.** *Federation Proceedings* 32(9):2010-2016.

This is a review with 81 references on the immunological effects of pesticides. Sensitization to high doses of pesticides as evidenced by dermatitis, production of antisera responsive to protein conjugates of pesticides, and the effect of pesticides on immunologically controlled defense mechanisms are discussed.

Pesticides

46
Eremeeva, L. S.; Trikulenko, V. I. 1976. **An experimental study of the sensitizing properties of a series of surfactants in cutaneous entrance into the body.** *Gigiena Truda i Professional'nye Zabolevaniya* 9:50-51.

To determine the effects of cation-active four-component ammonia compounds used in the textile and chemical industries and as additives to laundry products, tests were done on catamine AB, alcamone DS, and alkyldimethylamine oxide. Multiple applications to the skins of albino rats and guinea pigs caused sensitization and allergic contact dermatitis in rats. To evaluate the allergic reactions induced by chemicals, particularly surfactants which enter the body through the skin, leukocyte agglomeration, immunocompetent cell determination, and lysis are suggested.

Alcamone DS; Alkyldimethylamine oxide; Catamine AB

GUINEA PIGS; RATS

47
Ermakova, N. G. 1977. **Evaluation of T-lymphocyte populations of people under the effect of beryllium compounds.** *Gigiena Truda i Professional'nye Zabolevaniya* 10:52-54 (RUS).

The population of T-lymphocytes was estimated in spontaneous rosette formation tests, based on the decrease in the amount of rosette-forming T-lymphocytes in the blood of people with cell-immunity defects. The spontaneous rosette formation test was recommended for studying the pathogenesis of berylliosis, evaluating immunological status of people suffering from berylliosis, and the cure efficiency.

Beryllium

HUMAN STUDIES

48
Ermakova, N. G.; Vasileva, E. V. 1978. **Determination of the T- and B-lymphocytes in workers exposed to the effect of the chemical allergen beryllium.** *Gigiena Truda i Professional'nye Zabolevaniya* 4:32-35 (RUS).

T-, B-, and O-cells and lymphocytes forming rosettes with autologous erythrocytes were determined in workers exposed to beryllium and in patients with berylliosis; the exposed group and patients in remission had increased counts and a greater functional activity of the rosette-forming cells.

Beryllium

HUMAN STUDIES

49
Evdokimov, E. S. 1974. **Effect of organochlorine pesticides on animals.** *Veterinariya (Moscow)* 12:94-95 (RUS).

When administered orally to rats for 10 days, DDT (0.5 g/kg/day) or hexachlorocyclohexane (1 g/kg/day) decreased body weight gains, leukocyte and erythrocyte counts in the blood, and leukocyte phagocytic activity.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Lindane; Cyclohexane, 1,2,3,4,5,6-hexachloro-, (1alpha,2alpha,3beta,4alpha,5alpha,6beta)-

RATS

50
Faith, R. E.; Luster, M. I. 1977. **Modulation of immune function by chemicals of environmental concern.** *Environmental Health Perspectives* 20:245-246.

In studies undertaken to examine the effects of selected environmental chemicals on immune competence, experimental animals were exposed either prenatally, postnatally, or pre- and postnatally to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), polybrominated biphenyls (PBB), lead, and diethylstilbestrol (DES).

Diethylstilbestrol; Phenol, 4,4'-(1,2-diethyl-1,2-ethenediyl)bis-, (E)-; Lead; Polybromobiphenyl compounds; TCDD, 2,3,7,8-

51
Faith, R. E.; Moore, J. A. 1977. **Impairment of thymus-dependent immune functions by exposure of the developing immune system to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).** *Journal of Toxicology and Environmental Health* 3(3):451-464.

The effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on the developing immune system were investigated in F344 rats. Fetal and neonatal rats were exposed to TCDD through maternal dosing (5 ug/kg) on day 18 of gestation and on days 0, 7, and 14 of postnatal life (group I). Another group of neonatal rats was exposed to TCDD through maternal dosing on days 0, 7, and 14 of postnatal life only (group II). Body weight and thymus/body weight ratios were suppressed up to 145 days of age in group I, but only up to 39 days of age in group II. TCDD suppressed cell-mediated immune function without affecting humoral immune function. Suppression of T-cell function was selective in that helper-cell function was not suppressed.

TCDD, 2,3,7,8-

RATS

52
Fan, A., Street, J. C.; Nelson, R. M. 1978. **Immune suppression in mice administered methyl parathion and carbofuran by diet.** *Toxicology and Applied Pharmacology* 45(1):235.

Following a four week diet treatment of 0, 0.08, 0.7, or 3.0 mg methyl parathion/kg/day; or 0, 0.1, 0.6, or 1.0 mg carbofuran/kg/day, groups of Swiss (ICR) mice were administered a single LD50 dose of S. typhimurium C5' cells i.p. Active immunity was induced in some by a weekly injection of S. typhimurium during pesticide treatment. Dose-related mortality associated with increased bacteria in blood, decreased total specific immunoglobulins and c-globulins in serum, and reduced splenic blast formation in response to mitogens were observed. Pesticide diet treatment decreased immunization protection. Cellular sensitivity to dinitrofluorobenzene was not affected.

Methyl parathion; Phosphorothioic acid, O,O-dimethyl O-(4-nitrophenyl) ester; Carbofuran; 7-Benzofuranol, 2,3-dihydro-2,2-dimethyl-, methylcarbamate

MICE

53
Farber, T.; Kasza, L.; Giovetti, A. 1978. **Effect of polybrominated biphenyls (Firemaster BP-6) on the immunologic system of the beagle dog.** *Toxicology and Applied Pharmacology* 45(1):343.

Male dogs were administered 0, 0.0625, 0.25, 1.0, and 4.0 mg/kg of Firemaster BP-6 orally for 61 days. Blood smears taken at the 30th and 61st day revealed juvenile lymphocytes along with cells that appeared to be generating lymphocytes in some dogs at all levels, particularly evident at the 0.25 and 1 mg/kg dose levels. Hematopoiesis was markedly reduced in bone marrow of the 4 mg/kg group, and a marked increase in large reticuloendothelial cells with foamy cytoplasm occurred. Three of six dogs at the 1 mg/kg level showed similar changes but to a much lesser extent. Lymph nodes at the 4 mg/kg level showed variable degrees of depletion of lymphocytes, particularly in the T-cell zone, which were minimal at the 1 mg/kg level. In dogs at the 4 mg/kg level, marked extramedullary hematopoiesis, predominantly of a erythropoietic and megakaryopoietic nature, existed in the spleen, and lymphocytes were moderately reduced in the white pulp. At the 1 mg/kg level, extramedullary hematopoiesis was mild to minimal. A varible degree of involution of thymic tissue occurred at all dose levels. Anti-dog IgG fluorescein-conjugated rabbit antibody determined the distribution of plasma cells in the popliteal lymph node. Plasma cell numbers of dogs at the 4 mg/kg level were markedly reduced compared with those of the control group.

Polybromobiphenyl compounds

DOGS

54
Felsenstein, W. C.; Prather, J. C.; Gardner, D. E.; Coffin, D. L. 1974. **Effects of NO2 on humoral immunologic defense mechanisms.** *Toxicology and Applied Pharmacology* 29(1):80.

Increased susceptibility to pulmonary infections after exposure to NO2 and other oxidant air pollutants is documented in animals. The factors responsible are not well-understood, especially with respect to humoral immune defense mechanisms. Following a 1-hr exposure to 10 ppm NO2, blood samples were obtained from giant Flemish rabbits and Balb C mice. Immunoglobulins and complement, measured as the C3 fraction, were determined in rabbits; only immunoglobulins were measured in mice. The immunoassay employed was electro-immunodiffusion. C3 levels in NO2-exposed rabbits were not significantly different from controls. Slight drops in IgA and IgM with little change in IgG levels were noted. Mice showed moderate to three-fold increases in IgA and IgG, respectively, and moderate to slight decreases for IgG2 and IgM.

Nitrogen oxide

RABBITS; MICE

55
Fenters, J. D.; Bradof, J. N.; Aranyi, C.; Ketels, K.; Ehrlich, R.; Gardner, D. E. 1979. **Health effects of long-term inhalation of sulfuric acid mist-carbon particle mixtures.** *Environmental Research* 19(2):244-257.

Immunological effects following exposure of mice to 1.5 mg/cu m carbon particles or a mixture of 1.5 mg/cu m carbon particles with 1.4 mg/cu m sulfuric acid were investigated. The immune status of the animals was studied directly by the primary response of spleen cells following specific antigen stimulation and indirectly by infectivity studies. Determination of serum immunoglobin concentrations was employed as a quantitative measure of effects on the immune system without antigenic stimulation. Depression of primary antibody response to spleen cell antigenic stimulation; significant alterations in immunoglobulin titer; and decreased resistance to respiratory infection as measured by pulmonary consolidation, survival time, and mortality after 20 weeks exposure to the mixture were noted. Reduced bactericidal capacity was observed in the lungs of animals exposed to the carbon particles alone or to the mixture. It is suggested that prolonged exposure to low concentrations of sulfuric acid and carbon particle mixtures reduces the ability of mice to resist the secondary stress of respiratory infection.

Sulfuric acid; Carbon

MICE

56
Filippova, Z. K. 1972. **The role of the reticuloendothelial system in developing immunity to industrial poisons.** *Trudy Ufimskogo Nauchno-Issledovatel'skogo Instituta Gigieny i Profzabolevanii* 7:98-103.

57
Frash, V. N.; Karaulov, A. V.; Yushkov, B. G. 1977. **Leukosis-promoting effect of benzene (state of stem and immunocompetent cells under the effect of small doses of benzene).** *Rol. Stvolovykh Kletok Leikozo-Kantserogeneze*, ed. R. E. Kavetskii, pp. 79-80 (RUS). Kiev, USSR: Akad. Nauk Ukr. SSR.

When inhaled repeatedly in small doses over a four-month period in adult mice or during the first two weeks by newborn mice, benzene induced preleukotic changes in the blood, spleen, thymus, and bone marrow.

Benzene

MICE

58
Fridman, G. I. 1967. **Effect of Sevin, chlorophos, and DDT on some specific and nonspecific indexes of the immunobiological and general reactivity of an organism (problem of toxic actions of low intensity).** *Vop. Gig. Toksikol. Pestits.*, ed. G. V. Vygodchikov, pp. 139-145 (RUS). USSR: Tr Nauch. Sess. Akad. Med. Nauk SSSR.

The actions of pesticides of low toxicity (Sevin, chlorophos, DDT) on living organisms were studied. Administration of these pesticides, particularly DDT, in doses inducing no external toxic manifestations, led not only to a suppression of both general and immunobiological reactivity of the organism but also to distinct phase variations of the examined specific and nonspecific indices of reactivity. The observed changes followed a sinusoidal curve indicating an autoregulatory process of restoration of the disturbed functional condition.

Chlorophos; Phosphonic acid, (2,2,2-trichloro-1-hydroxyethyl)-, dimethyl ester; DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Carbaryl; 1-Naphthalenol, methylcarbamate

59
Fritz, J.; Ludvan, M. 1978. **Recent data on chromium and nickel allergies.** *Zeitschrift fuer Hautkrankheiten* 53(15):531-536 (GER).

From 1972 until April 1977 contact allergy to chrome and/or nickel was established in 143 women and 88 men using epicutaneous testing. In addition, 31 patients with nickel allergy and 17 patients with chrome allergy were examined using the leukocyte migration inhibition test. Potassium dichromate, chromium chloride, chromium sulfate, and nickel sulfate were employed as antigens. When the same antigens in the same concentrations were employed, results from the Nicholl's leukocyte aggregation test correlated closely with data from the migration inhibition test.

Chromium chloride; Chromium sulfate; Nickel sulfate; Potassium dichromate

HUMAN STUDIES

60
Gabliks, J.; Al-Zubaidy, T.; Askari, E. 1975. **DDT and immunological responses. 3. Reduced anaphylaxis and mast cell population in rats fed DDT.** *Archives of Environmental Health* 30(2):81-84.

Rats immunized with diphtheria toxoid and fed diets containing DDT at 20 and 200 ppm for 30 days did not show effects on their serum antitoxin titers, but the numbers of metachromatically stained, histamine-containing mast cells in mesenteries were decreased. Severity of anaphylactic shock was also decreased in proportion to the dietary levels of DDT, and, thus, the magnitude of the shock correlated with the numbers of mast cells. Apparently, daily dietary intake of greater than 2.2 mg/kg alters the physiology of mast cells in the rat and thus affects histamine-mediated reactions.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

RATS

61
Gabliks, J.; Askari, E. M.; Yolen, N. 1973. **DDT and immunological responses. I. Serum antibodies and anaphylactic shock in guinea pigs.** *Archives of Environmental Health* 26(6):305-308.

This article describes the effects of DDT on antibody synthesis and anaphylactic shock in guinea pigs immunized with diphtheria toxoid. During the prolonged administration of DDT, no toxic effects were observed and no gross anatomical changes in organs were noted upon autopsy. The primary immune response, assessed by the protective immunity against toxin, serum antitoxin titers, and increases in gamma-globulin fraction, was not altered in guinea pigs receiving (15 mg/kg) injections beginning 7 to 14 days prior to the immunization and for 14 or 21 days thereafter. However, when control and DDT-treated animals were injected with a second (shocking) dose of diphtheria toxoid 30 days after immunization, classical symptoms of anaphylactic shock, frequently resulting in death, were seen. However, control groups consistently showed a more severe reaction than did the DDT-treated animals. This reduced severity of anaphylactic shock following long-term administration of DDT (44 days) was noted in six separate experiments. It was hypothesized that DDT interferes with a factor(s) involved in the mechanism of anaphylaxis.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

GUINEA PIGS

62
Garcia, I.; Rylander, R. 1977. **Pulmonary humoral immune response after exposure to carbon monoxide.** *Schweizerische Medizinische Wochenschrift* 107(6):203-205.

Using the plaque-forming cell technique, the effect of exposure to CO was studied in guinea pigs. Exposure to 200 ppm for five weeks was found to reduce the capacity to produce IgG and IgM in free lung cells.

Carbon monoxide

GUINEA PIGS

63
Gaworski, C. L.; Sharma, R. P. 1977. **Heavy metals and lymphocytes: a possible site of immunosuppression by chemicals.** *Toxicology and Applied Pharmacology* 41(1):149.

Heavy metals have been shown to be immunosuppressive, a characteristic that may intimately involve lymphocytes. The effects of lead, cadmium, mercury, and zinc were determined on the response of lymphocyte cell cultures to stimulation by mitogens and membrane ATPase activity from mice exposed to various concentrations of these metals in drinking water for 30 days. Splenic lymphocytes were cultured at 15 to 30 days to determine the response to phytohemagglutinin and pokeweed mitogen by measuring the uptake of (3H)thymidine. In vitro response was measured by adding the metals directly to the cell cultures. Results suggest that these metals produce an effect directly on the lymphocyte cells and that one site of interaction may be related to the ATPase enzyme located on the membrane.

Cadmium; Lead; Mercury; Zinc

MICE

64
Gaworski, C. L.; Sharma, R. P. 1978. **The effects of heavy metals on (3H)thymidine uptake in lymphocytes.** *Toxicology and Applied Pharmacology* 46(2):305-313.

Effects of cadmium, lead, mercury, and zinc on the response of mouse splenic lymphocyte cultures to stimulation by phytohemagglutinin (PHA) and pokeweed mitogen (PWM) were determined. Mice were exposed for 30 days to the metal salt in the drinking water. At 15 and 30 days splenic lymphocytes were cultured and response to the mitogens measured following addition of the metal salts to the culture. In vivo exposure to high concentrations of lead, cadmium, or mercury for 30 days significantly reduced responses to both mitogens. Decreases were noted following 15 days exposure to cadmium (1.42mM) and mercury (0.50mM). In vitro cadmium and mercury also produced dose-dependent inhibition, with a more sensitive response to PHA. Results suggest that these metals may affect the lymphocyte directly by altering synthesis of cellular DNA and

thereby influencing antibody production. All metals used caused a dose-dependent inhibition of oubain-insensitive ATPase in isolated lymphocytes.

Lead; Cadmium; Zinc; Mercury

MICE

65
Giurgea, R.; Witterberger, C.; Frecus, G.; Manciulea, S.: Borsa, M.; Coprean, D.; Ilyes, S. 1978. **Effects of some organochlorine pesticides on the immunological reactivity of white rats.** *Archiv fuer Experimentelle Veterinaermedizin* 32(5):769-774 (GER).

Following daily administration of aldrin or lindane at 8 or 11 ppm in the diet, Wistar rats were inoculated with E. coli and the capacity to form antibodies compared with that of controls. Antibody formation at 90 and 150 days was not inhibited, but changes were noted, as were functional disorders of the adrenal glands, thymus, and protein synthesis. Aldrin (LD50 = 300 ppm) was more toxic than lindane (LD50 = 150 ppm), and younger animals were more strongly affected. These pesticides caused marked changes in the immunological reactivity of these animals even at the very small doses used.

Aldrin; 1,4:5,8-Dimethanonaphthalene, 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-, (1alpha,4alpha,4abeta,5alpha,8alpha,8abeta)-; Lindane; Cyclohexane, 1,2,3,4,5,6-hexachloro-, (1alpha,2alpha,3beta,4alpha,5alpha,6beta)-

RATS

66
Glick, B. 1974. **Antibody-mediated immunity in the presence of mirex and DDT.** *Poultry Science* 53(4):1476-1485.

To evaluate the effects of mirex and DDT on the immune system of chickens, animals were fed doses of these compounds. Body weight, organ weights (bursa, spleen, adrenal, thymus, liver), levels of IgG or IgM, antibody response to bovine serum albumin as measured by precipitin levels, and number of plaque-forming cells to sheep red blood cells were not affected by feeding 200-400 ppm mirex for up to five weeks of age. Levels of IgG and IgM were significantly depressed in animals fed 500 ppm of mirex; however, antibody production was not affected. Data from these studies and from experiments in which feed was withdrawn prior to administration of bovine serum albumin for the precipitin assay indicate that chickens exposed to high levels of these chemicals and faced with other environmental changes are less able to mount a normal antibody response.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Mirex; 1,3,4-Metheno-1H-cyclobuta(cd)pentalene, 1,1a,2,2,3,3a,4,5,5,5a,5b,6-dodecachlorooctahydro-

CHICKENS

67
Gorbachevskaia, E. F. 1980. **Effect of chronic poisoning with the gamma isomer of hexachlorocyclohexane on antibody formation.** *Gigiena i Sanitariya* (1):72-73 (RUS).

Chronic administration of gamma-hexachlorocyclohexane to rabbits (4 mg/kg, daily for three months) caused the animals to be anemic. The animals had immunogenic stress. The number of erythrocytes, total Hb, reticulocyte and platelet forming cells at the end of three month period were practically similar to the starting period.

Lindane; Cyclohexane, 1,2,3,4,5,6-hexachloro-, (1alpha,2alpha,3beta,4alpha,5alpha,6beta)-

RABBITS

68
Graham, J. A.; Gardner, D. E.; Miller, F. J.; Daniels, M. J.; Coffin, D. L. 1975. **Effect of nickel chloride on primary antibody production in the spleen.** *Environmental Health Perspectives* 12:109-113.

Mice immunized intraperitoneally with sheep erythrocytes were treated with nickel chloride, a common particulate air pollutant, and primary antibody production in the spleen examined using a hemolytic plaque technique. A negative linear dose-response relationship was observed between the logarithm of plaques/10(6) cells and the nickel concentration administered. Mice injected with 3.09 ug Ni(2+)/g body weight displayed lymphocyte function similar to that of control mice. However, injection of 9.26-12.34 ug Ni(2+)/g caused significant immunosuppression.

Nickel chloride

MICE

69
Graham, J. A.; Miller, F. J.; Daniels, M. J. 1978. **Influence of cadmium, nickel, and chromium on primary immunity in mice.** *Environmental Research* 16(1-3):77-87.

Using a hemolytic plaque technique to determine the number of specific antibody-producing spleen cells, the effects of cadmium, nickel, and chromium on the primary humoral immune system of mice were investigated. Inhalation of nickel chloride (NiCl2) for two hr resulted in a significant negative linear dose response. A significant reduction in the number of plaques/10(6) cells also was observed with exposure to 190 ug Cd/cu m. Analyses of the data from mice exposed i.m. indicated that concentrations 03.90 ug Ni/g body weight (as NiSO4) and 9.25 ug Ni/g body weight (as NiCl2) resulted in significant immunosuppression. Intramuscular treatments with nickel oxide, chromic chloride, and cadmium chloride had no effect at the concentrations tested.

Cadmium; Nickel; Chromium; Cadmium chloride; Nickel chloride; Nickel oxide; Chromium chloride

MICE

70
Graham, T. M.; Morris, J. E. 1978. **Primary immune response in dogs exposed to 239PuO2.** *Health Physics* 35(6):888.

Inhaled plutonium oxide induces a time- and dose-dependent lymphopenia prior to tumor appearance in dogs. Exposed and unexposed dogs were immunized by i.v. with key hole limpet hemocyanin to measure the effects of inhaled plutonium on the humoral component of the immune system. Antibody levels in blood were measured with a direct binding and precipitating radioimmunoassay. Antibody precipitation curves indicated that inhaled Pu induced a significant functional decrease in the primary antibody response of exposed dogs.

Plutonium oxide; Benzo(a)pyrene

DOGS

71
Greene, N. D.; Schneider, S. L. 1978. **Effects of nitrogen dioxide on the response of baboon alveolar macrophages to migration inhibitory factor.** *Journal of Toxicology and Environmental Health* 4(5/6):869-880.

Pulmonary alveolar macrophages (PAM) were obtained by lavage from baboons exposed for six months to 2 ppm NO2 for eight hr a day, five days a week, and the response of these cells to autologous migration inhibitory factor (MIF) was determined. PAM from two or three antigen-sensitized, NO2-exposed animals failed to respond to MIF derived from antigen-stimulated autologous lymphocytes. Similarly, PAM from three of the four NO2-exposed animals had diminished responsiveness to MIF obtained by phytohemagglutinin stimulation of their own lymphocytes. The altered responsiveness resulted from an effect on the macrophages and not on the lymphocytes used to prepare the MIF, as shown by the normal blastogenic responsiveness of the lymphocytes and the normal activity of the MIF thus produced on guinea pig peritoneal macrophages. Thus, inhalation of 2 ppm NO2 may have important subtle effects on pulmonary cells, which may result in altered immune capabilities within the lung.

Nitrogen oxide

BABOON

72
Gudina, R. V. 1976. **Specific sensitization to some chemicals used in the textile industry.** *Gigiena Truda i Professional'nye Zabolevaniya* 7:14-17 (RUS).

Precipitating antibodies to chemical allergens in the textile industry were studied. Experiments conducted with 20 rabbits demonstrated specific antibody formation which showed characteristic features of the immune response confirming the specificity and sensitivity of the modified method for determining antihaptenic antibodies. Specific sensitization in workers occupationally exposed to chemical allergens and its relationship with clinical manifestations of dermatosis were noted following an examination of 146 persons.

RABBITS; HUMAN STUDIES

73
Hinsdill, R. D.; Thomas, P. T. 1978. **Effect of polychlorinated biphenyls on the immune responses of rhesus monkeys and mice.** *Toxicology and Applied Pharmacology* 44(1):41-51.

Female rhesus monkeys were fed chow containing 2.5 or 5.0 ppm of Aroclor 1248 (PCB). After six months, the PCB-fed monkeys developed alopecia, chloracne, and facial edema. After 11 months, control and treated monkeys were immunized with sheep red blood cells (SRBC) and tetanus toxoid (TT). Monkeys fed 5.0 ppm of PCB had significantly lower anti-SRBC antibody titers than controls at only two intervals following primary immunization. Antibody response to TT was not measurably affected by PCB exposure. Both PCB-fed groups had consistently lower gamma-globulin levels than controls. These results indicate that sustained exposure to low levels of PCB could have modest to slight immunosuppressive effects, which might be important depending on the general health of the individual. Mice fed about 1,000 ppm of PCB for three to five weeks exhibited no signs of PCB intoxication other than liver hypertrophy. When these mice were challenged with Salmonella typhimurium, however, they showed higher mortality and significantly greater numbers of viable organisms in the spleen, liver, and blood than did controls. Exposed mice also showed an increased sensitivity to endotoxin. Thus, mice exposed to subclinical doses of PCB appear to have an impaired ability to withstand challenge by pathogens and an increased sensitivity to endotoxin.

Polychlorobiphenyl compounds

MICE; MONKEYS

74
Hirokawa, K.; Hayashi, Y. 1980. **Acute methylmercury intoxication in mice-effect on the immune system.** *Acta Pathologica Japonica* 30(1):23-32.

The effect of organic mercury on the immune system was studied in experimental acute methylmercury intoxication in mice. Marked atrophy of the thymic cortex and splenic lymphoid follicles associated with decrease of PHA(phytohemagglutinin)- and LPS(lipopolysaccharide)-responsiveness of splenic lymphocytes and conversely increased PHA- and LPS-responsiveness of thymocytes were observed after seven daily injections of methylmercury hydroxide. An apparent decrease of antibody formation against sheep red blood cells was observed at seven days after the last injection. All changes reverted to normal levels within four weeks after the last injection. Histochemically, massive mercury deposits were found in the renal tubules and slight deposits in macrophages throughout the body at seven days after the last injection. The mercury deposits in macrophages of the thymus, lymph nodes, and liver increased in concentration thereafter, with concomitant decrease of those in renal tubules. Organic mercury may show a direct cytotoxic effect on lymphocytes, but the effect may soon be detoxicated by macrophages.

Methylmercury

MICE

75
Holt, P. G.; Finlay-Jones, L. M.; Keast, D.; Papadimitrou, J. M. 1979. **Immunological function in mice chronically exposed to nitrogen oxides.** *Environmental Research* 19(1):154-162.

BALB/c mice were exposed to 10 ppm nitrogen oxide or nitrogen dioxide for two hr daily for periods up to 30 weeks. At seven week intervals, groups of animals were subjected to a variety of pathological and immunological examinations–serum antibody responses to T-dependent and T-independent antigens, spleen cell phytohemagglutinin, hemagglutinin, graft-vs-host responses, routine hematology, capacity to reject a transplanted tumor, and lung pathology. Tests of immune function indicated suppression resulting from chronic exposure to these gases, and in most cases data indicated enhancement of immunological reactivity by shorter exposures. Nitrogen dioxide appeared somewhat more potent than nitrogen oxide in this regard, but the differences observed were not great. Chronic nitrogen oxide exposure produced a more severe lung pathology, with clear evidence of paraseptal emphysema.

Nitrogen oxide

MICE

76
Holt, P. G.; Keast, D. 1977. **Environmentally induced changes in immunological function: acute and chronic effects of inhalation of tobacco smoke and other atmospheric contaminants in man and experimental animals.** *Bacteriological Reviews* 41(1):205-216.

Exposure of experimental animals to a variety of chemically unrelated agents precipitates a characteristic pattern of change in immunological function. Dosages required to cause these effects are low (especially when exposure time is high), and it would appear that altered immune capacity may prove one of the most sensitive biological indices of the toxicity of atmospheric contaminants. Many airborne substances have potential for both immunosuppression and immunostimulation, depending upon dosage schedule. Available data from experimentation on humoral and cellular immune function in human smokers parallel those from animal models in many respects.

Tobacco

HUMAN STUDIES

77
Holt, P. G.; Keast, D., Mackenzie, J. S. 1978. **Animal model of human disease: infections and neoplastic respiratory diseases associated with cigarette smoking.** *American Journal of Pathology* 90(1):281-284.

Mice exposed to the smoke of cigarettes exhibit biphasic changes in local and systemic immune function. Antibody production within the lung is severely depressed within two weeks of starting exposure. In contrast, the regional lymph node and systemic activity show transient enhancement as long as 16 weeks during continuous exposure prior to eventual suppression. Cellular immunity exhibits similar temporal changes. This biphasic phenomenon has also been observed in challenge experiments involving live influenza virus and viable tumor cells. Similar immunologic changes are also demonstrable following long-term exposure to industrial air pollutants. Likely, the agents in tobacco smoke which produce immunosuppression are chemically similar to industrial air pollutants (particularly nitrogen oxides). Immunologic function in man is probably also affected by long-term inhalation of cigarette smoke. Smokers have an increased susceptibility to influenza and other respiratory infections; antibody titers following immunization with killed influenza vaccines fall more rapidly in smokers than in nonsmokers, provided they have little or no immunity before vaccination; lymphocytotoxic antibody production against HLA antigens during consecutive pregnancies is less marked in smoking mothers; smokers consistently exhibit leukocytosis; alveolar macrophages from cigarette smokers fail to respond to the lymphokine MIF; and chemotaxis is depressed in smokers. It has been suggested that a transient enhancement in some T-lymphocyte function similar to that observed in the mouse may also occur in human smokers. It is unlikely that carcinogenic tobacco tars play a significant role in the etiology of infectious respiratory diseases in smokers; however, cigarette smoke contains many carcinogens, which may induce lung cancer. Tobacco smoke components other than tars may also be harmful to the health of smokers. Immunologic mechanisms similar to those which provide host protection against infectious diseases may also play a role in providing host protection against the development and spread of neoplastic conditions. Immunosuppression caused by prolonged cigarette smoking may therefore be involved in the etiology and pathogenesis of diseases associated with this habit.

Tobacco

HUMAN STUDIES; MICE

78
Huuskonen, M. S.; Rasanen, J. A.; Harkonen, H.; Asp, S. 1978. **Asbestos exposure as a cause of immunological stimulation.** *Scandinavian Journal of Respiratory Diseases* 59(6):326-332.

Immunological parameters were determined for 37 asbestos-exposed workers with no radiographic pulmonary fibrosis and 132 asbestosis patients, 37 of whom formed a matched referent group for the non-diseased workers. No clear differences between the matched groups were found for the autoantibodies tested, but autoantibody prevalence was increased in both groups in comparison with Finnish blood donor candidates. A general immunological activity caused by asbestos dust may act as an adjuvant in immunization. The patients showed high levels of IgA, C3, C4 and alpha-1-antitrypsin. These factors may be related to the development of asbestosis and could therefore be utilized in the evaluation of diffuse pulmonary fibrosis among workers exposed to asbestos.

Asbestos

HUMAN STUDIES

79
Hyslop, N. S. 1978. **Immunological aspects of environmental contamination.** *International Symposium on Microbial Ecology*, CPI 5(11), reg. no. B773086. Heidelberg: Springer-Verlag.

80
Karol, M. H.; Alarie, Y. C. **Respiratory anaphylaxis to industrial chemicals.** Research at University of Pittsburgh, Department of Industrial and Environmental Health Sciences, Pittsburgh PA; Sponsored by DHEW, Research Triangle Park NC, code R01 ES 01532-03; 4/77-3/80.

An animal model of respiratory hypersensitivity to industrial chemicals has been developed in guinea pigs. Repeated exposure to antigen aerosols containing hapten-protein conjugates results in pulmonary sensitization and antibody production to the haptenic portion of the antigens. Sensitivity to both aliphatic and aromatic chemicals has been achieved using this procedure. Proposed research will be directed toward inducing pulmonary sensitization in guinea pigs by repeated exposure to vapors of industrial chemicals. Sensitization will be assessed by: increased respiratory rate, bronchial constriction, and specific antibody formation. If successful, chemicals known to have allergenic abilities in man will be used for animal sensitization. Allergenic potencies of industrial chemicals can be evaluated in the guinea pig and then compared to their reported potencies in man. These comparisons allow assessment of the value of the guinea pig as an animal model for pulmonary sensitization of man. Research will also focus on use of hapten-protein conjugates to detect hapten-specific IgE antibodies in sensitized industrial workers. Evaluation of sera from additional workers will indicate the potential applicability of such serologic tests for pre-employment screening of industrial workers.

GUINEA PIGS; HUMAN STUDIES

81
Karol, M. H.; Ioset, H. H.; Alarie, Y. C. 1979. **Effect of coal dust inhalation on pulmonary immunologic responses.** *American Industrial Hygiene Association Journal* 40(4):283-290.

Guinea pigs exposed to a coal dust aerosol (200 mg/cu m for one hr/day, five days/week) for four weeks were evaluated for hypersensitivity. From analyses of respiratory rates, no evidence of immediate pulmonary sensitivity was obtained. To assess the possible activity of coal dust as an adjuvant, the effect of coal dust accumulation in the lungs on the induction of subsequent respiratory hypersensitivity to an unrelated antigen was investigated. Coal-exposed and control guinea pigs were sensitized to the antigen p-azobenzene arsonate ovalbumin by inhalation. Both groups developed severe pulmonary hypersensitivity to the antigen. There was no difference between the groups with regard to the severity of the hypersensitivity responses, the frequency of such responses, or the amounts of antibodies produced by both groups of animals. Pulmonary alveolar macrophages isolated from coal-exposed guinea pigs had only 0.33 the protein-synthesizing ability of macrophages from control animals.

Coal

GUINEA PIGS

82
Karol, M. H.; Sandberg, T.; Riley, E. J.; Alarie, Y. 1979. **Longitudinal study of tolyl-reactive IgE antibodies in workers hypersensitive to TDI.** *Journal of Occupational Medicine* 21(5):354-358.

Three workers with TDI hypersensitivity were evaluated for IgE antibodies to TDI. A radioallergosorbent test system was

employed using p-tolyl(mono)isocyanate-human serum albumin antigen covalently bound to cyanogen bromide-activated paper discs. In two individuals who experienced several bronchial hypersensitivity responses to TDI during the study period, IgE antibody titers were consistently elevated. The responses were either solely asthmatic or asthmatic accompanied by cutaneous hypersensitivity reactions. By contrast, antibody titers in a third subject who had not experienced any hypersensitivity reactions during the study period continually decreased, falling to insignificant levels after 12 months. In the absence of renewed TDI exposure, sensitive workers may have titers indistinguishable from those of workers exposed to TDI but without sensitivity to the chemical.

Toluene diisocyanate; Benzene, 1,3-diisocyanatomethyl-

HUMAN STUDIES

83
Kately, J. R.; Bazzell, S. J. 1978. **Immunological studies in cattle exposed to polybrominated biphenyls.** *Environmental Health Perspectives* 23:75-82.

A study of cattle exposed to polybrominated biphenyls (PBBs) revealed no hematological or immunological changes, no evidence of autoantibodies, and no cytotoxic or immunosuppressive effects. Thus, exposure to PBBs does not interfere with lymph surface antigens, the complex nuclear and cytoplasmic events required for mitosis and cell division, or the events required for antibody formation and cell-mediated immune reactions.

Polybromobiphenyl compounds

CATTLE

84
Kazantzis, G. 1978. **The role of hypersensitivity and the immune response in influencing susceptibility to metal toxicity.** *Environmental Health Perspectives* 25:111-118.

Immune responses can be mediated either by the action of humoral antibodies or by specifically sensitized lymphocytes and classified as follows: anaphylactic or immediate hypersensitivity; cytotoxic hypersensitivity; cell-mediated hypersensitivity, or immune complex hypersensitivity. The commonly occurring clinical effects from increased cellular reactivity to Pt, Au, Hg, Cr, Ni, and Be are conjunctivitis, rhinitis, asthma, urticaria, contact dermitis, nephrotic syndrome, blood dyscrasia, or proteinuria. Cutaneous hypersensitivity is the most common, affecting industrial and general populations. In addition, metal compounds used in therapeutics and in prostheses have induced hypersensitive reactions.

Platinum; Mercury; Gold; Nickel; Chromium; Beryllium

85
Kerkvliet, N. I.; Koller, L. D. 1978. **Modification of tumor growth and cell-mediated cytotoxic immune responses by exposure to environmental contaminants: effects of cadmium and polychlorinated biphenyls (Aroclor 1254.)** *RES Journal of the Reticuloendothelial Society* 24(Suppl):1A.

Cadmium; Polychlorobiphenyl compounds

86
Kimbrough, R.; Buckley, J.; Fishbein, L.; Flamm, G.; Kasza, L.; Marcus, W.; Teske, R. 1978. **Animal toxicology.** *Environmental Health Perspectives* 24:173-184.

Recent data on the toxic effects of PCBs in mammals and birds are summarized. Chronic toxic effects are emphasized. Subacute and reproductive effects of PCBs, PBBs, and chlorinated dibenzofurans in mammals are reviewed. Toxicity of chlorinated and brominated dibenzofurans in mammals and toxicity of chlorinated dibenzofurans in avian species are investigated. Other topics include: long-term toxicity and tumorigenesis, immunosuppressive effects of PCBs and PBBs, mutagenicity and teratology of PCBs and PBBs, and toxicity of naphthalenes in animals and in humans.

Dibenzofuran, chlorinated; Polybromobiphenyl compounds; Polychlorobiphenyl compounds; Dibenzofuran, brominated; Naphthalene

87
Klotz, V. I.; Babayants, R. A.; Brysin, V. G.; Safarova, A. A. 1978. **Effect of pesticides on the immunological reactivity of the body of animals and man.** *Gigiena i Sanitariya* (9):35-36 (RUS).

The titer of complement-connecting antibrucellosis antibodies circulating in the blood was determined in rabbits receiving a s.c. injection of brucellosis vaccine and in those receiving a 2 ml solution of DDT orally two days prior to immunization. In the control group antibodies were found on day five in a titer of 1:40, on day 15 at 1:640, and on days 20 to 30 at 1:320; antibodies decreased to 1:80 on day 60. In the DDT-treated group antibodies were not found until day ten at a very low titer of 1:20 rising to 1:160 on day 20, decreasing to 1:40 on day 40, increasing to 1:160 on day 50, and decreasing to 1:40 on day 60. The average titer of typhoid agglutinins in the blood serum of 24 of 50 people revaccinated s.c. with 1 ml typhoid vaccine, with no contact with poisonous chemicals, was 1:310 21 days after inoculation, 11.6 times higher than preinoculation, and 1:251 five months after immunization. In 26 people who work in contact with organophosphorus and organochlorine pesticides, the titer was 1:90 21 days after revaccination but only 1:54 five months later. The action of the poisonous chemicals may possibly cause significant discrepancy of the levels of postvaccine immunity.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

RABBITS; HUMAN STUDIES

88
Koller, L. D. 1979. **Effects of environmental contaminants on the immune system.** *Advances in Veterinary Science and Comparative Medicine* 23:267-295.

Alteration of the immune response due to indirect toxicity of environmental chemicals is reviewed. Due to its persistence in the environment and accumulation in animal tissues, emphasis is given to the effects of DDT. Animals exposed to DDT are frequently found to be more susceptible to infectious organisms than controls. Occasional inhibition of antibody response in animals previously exposed to DDT has been noted. A decrease in the numbers of plasma cells in popliteal lymph nodes has been observed following DDT exposure, as well as reduced germinal centers in the spleen and an inhibited skin sensitivity to tuberculin in rabbits. Other contaminants briefly mentioned in this review include heavy metals, industrial chemicals (PCBs, TCDD), and the pesticides lindane, dicresyl, Sevin (carbaryl), Tillam (pebulate), Jalan, maneb, chlorophos (trichlorfon), methylnitrophos (fenitrothion), warfarin, propanide (propanil), heptachlor, carbofuran, mirex, milbex, Anthio (formothion), paraquat, and Carbamine.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Pesticides

89
Koller, L. D. 1979. **Some immunological effects of lead, cadmium, and methylmercury.** *Drug and Chemical Toxicology* 2(1, 2):99-110.

Cadmium; Lead; Methylmercury

90
Koller, L. D. 1977. **Altered immune response by heavy metals.** *International Symposium on Clinical Chemistry and Chemical Toxicology of Metals: Abstracts,* n.p.

Metals

91
Koller, L. D. 1977. **Toxicological, pathological, and immunological effects of methylmercury in rabbits.** *International Symposium on Clinical Chemistry and Chemical Toxicology of Metals: Abstracts,* n.p.

Methylmercury

RABBITS

92
Koller, L. D. 1977. **Altered immune response by environmental contaminants.** *International Symposium on Pathobiology of Environmental Pollutants: Animal Models and Wildlife as Monitors,* CPI 5(9), reg. no. A772277. Storrs CT.

93
Koller, L. D. 1978. **Effects of environmental contaminants on cell-mediated immunity.** *U.S. NTIS Report* PB 292034, 37 pp.

The effect of lead and cadmium on cell-mediated immunity was studied in peritoneal macrophages, B-, and T-lymphocytes of mice. Lead and cadmium were administered in drinking water for ten weeks in short-term experiments and up to 18 months to examine immune responses in aged mice. Lead and cadmium both tended to stimulate phagocytosis in peritoneal macrophages. Consequently, depressed humoral immune response could not be explained on the basis of an effect on the macrophage. Both lead and cadmium treatment depressed the splenic B-lymphocyte response. The direct effect of these metals on B-cells could account, at least in part, for the suppression of the humoral immune response reported in previous studies. In long-term studies in aged mice, low doses of lead (13 mg/l) tended to stimulate certain immune responses. Results obtained with higher doses were complicated by a natural immunosuppression in aged mice. As a consequence, no significant alterations were observed with high doses; the impact of Pb on the immune system in the long term cannot be predicted on the basis of these experiments.

Lead; Cadmium

MICE

94
Koller, L. D.; Exon, J. H.; Arbogast, B. 1977. **Methylmercury: effect on serum enzymes and humoral antibody.** *Journal of Toxicology and Environmental Health* 2(5):115-123.

Dosages of 20 and 10 ppm methylmercury were toxic to rabbits while 1 ppm did not produce clinical signs or death. Serum alkaline phosphatase levels were elevated in all rabbits exposed to methylmercury. Methylmercury-exposed rabbits challenged to A PR8 influenza virus had hemagglutination inhibition titers as much as four times lower than those of controls. Histopathologic lesions were found in the cerebellum of rabbits that died. Thus, methylmercury chloride suppressed the humoral immune system and resulted in increased serum alkaline phosphatase levels, which may aid in diagnosis when methylmercury poisoning is suspected.

Methylmercury

RABBITS

95
Koller, L. D.; Exon, J. H.; Brauner, J. A. 1977. **Methylmercury: decreased antibody formation in mice.** *Proceedings of the Society for Experimental Biology and Medicine* 155(4):602-604.

Antibody synthesis was decreased in mice fed 1.5 or 10 ppm methylmercury for ten weeks. The primary immune response was significantly suppressed, while the secondary response was impaired but not significantly. Methylmercury apparently affects the B (bone marrow-derived)-cell or plasma-cell synthesis of Ig(immunoglobulin)M antibody.

Methylmercury

MICE

96
Koller, L. D.; Exon, J. H.; Roan, J. G. 1975. **Antibody suppression by cadmium.** *Archives of Environmental Health* 30(12):598-601.

Mice inoculated with antigen six weeks following discontinuance of exposure to subclinical doses of cadmium chloride for ten weeks showed a remarkable decrease in antibody-forming cells, particularly IgG levels. Data from this experiment indicate that immunosuppression produced following exposure to environmental chemicals may persist for several months following exposure.

Cadmium chloride

MICE

97
Koller, L. D.; Exon, J. H.; Roan, J. G. 1976. **Immunological surveillance and toxicity in mice exposed to the organophosphate pesticide, leptophos.** *Environmental Research* 12(2):238-242.

Mice were fed the organophosphate pesticide, leptophos, in feed at concentrations of 0, 10, 100, and 500 ppm for 12 weeks. Signs of organophosphate poisoning were moderate to severe inhibition of serum cholinesterase and decreased weight gains of leptophos-exposed mice. Primary and secondary immune responses as measured by hemolytic plaque assay of antibody-forming cells were not significantly altered in mice receiving leptophos. Histological lesions were not observed in mice which consumed as much as 170 mg leptophos/kg body weight a day for 12 weeks. Thus, leptophos does not significantly affect antibody formation and appears to be only slightly toxic to mice.

Leptophos; Phosphonothioic acid, phenyl-, O-(4-bromo-2,5-dichlorophenyl) O-methyl ester

MICE

98
Koller, L. D.; Isaacson-Kerkvliet, N.; Exon, J. H. 1979. **Synergism of methylmercury and selenium producing enhanced antibody formation in mice.** *Archives of Environmental Health* 34(4):248-252.

Mice fed 1, 5, and 10 ppm methylmercury and 6 ppm selenium for ten weeks showed a significant increase in antibody synthesis. Since methylmercury singly depresses antibody synthesis and the response was greater than that produced by selenium alone, synergism between methylmercury and selenium occurred. In tnis case, the synergism is considered to be advantageous to a host, while exposure by other combinations of environmental contaminants may be detrimental. These results indicate that data collected from individual pollutants may not be of value in predicting responses to multiple exposure.

Methylmercury; Selenium

MICE

99
Koller, L. D.; Kerkvliet, N. I. 1980. **Environmental contaminants-effects on tumor growth and immunity.** Research at Oregon State University, School of Veterinary Medicine, Corvallis OR; Sponsored by EPA, Washington DC, code R805210-03; 7/77-7/80.

The proposed study will determine the effects of arsenic and cadmium on the immune response of mice to a growing tumor and the effects of contaminant-induced immune alteration on the incidence and growth rate of tumors in exposed animals. Several parameters of immunity including serum-blocking activity, lymphocyte-mediated cytotoxicity, lymphokine production, and lymphocyte blastogenesis, will be assessed at various times after tumor inoculation. In addition, contaminant-exposed animals will be monitored for changes in in vivo tumor growth. Cadmium and arsenic, including sub-clinical doses, will be administered in the drinking water for 15 weeks prior to tumor inoculation and immune testing. A methylcholanthrene-induced and a Maloney virus-induced tumor system will be utilized to compare the differences in immune response to chemically induced and virus-induced tumors. A highly significant dose-dependent inhibition of GMSB-6 tumor growth was observed in Cd-exposed mice. The effect of Cd exposure on cell-mediated cytotoxicity was not apparent. Inhibition of cytotoxicity by Cd was not found.

Arsenic; Cadmium

MICE

100
Koller, L. D.; Roan, J. G. 1977. **Effects of lead and cadmium on mouse peritoneal macrophages.** *RES Journal of the Reticuloendothelial Society* 21(1):7-12.

Cadmium and lead given orally to mice for ten weeks stimulated phagocytosis and increased acid phosphatase levels in peritoneal macrophages. These environmental contaminants apparently activated macrophages. The effect of lead and cadmium on macrophage-related functions is discussed.

Cadmium; Lead

MICE

101
Koller, L. D.; Roan, J. G.; Kerkvliet, N. I. 1979. **Mitogen stimulation of lymphocytes in CBA mice exposed to lead and cadmium.** *Environmental Research* 19(1):177-188.

CBA mice were exposed to lead acetate or cadmium chloride in drinking water for ten weeks. Selected groups were also injected with Bacillus Calmette-Guerin (BCG) during exposure to the metals to determine response to BCG by in vitro stimulation with a purified protein of that antigen (PPD). The ability of mitogens concanavalin A (Con A) and lipopolysaccharide (LPS) to induce proliferation of splenic lymphocytes was also assessed. Lead tended to inhibit lymphocyte proliferation by LPS and PPD while cadmium potentiated blastogenesis by these mitogens. The two larger doses of cadmium, 30 and 300 ppm, resulted in intense proliferation which was significant for the non-BCG, 300-ppm cadmium group. However, 3 ppm cadmium reduced the lymphocyte response to LPS and PPD which was significant for the non-BCG-injected mice. Lead and cadmium did not significantly affect the response of lymphocyte proliferation by Con A.

Lead; Cadmium

MICE

102
Kosutzky, J. 1977. **Relations of persistent foreign substances to the immunologic reactivity of the organism (pesticides).** *Veterinarstvi* 27(10):467-468.

Pesticides

103
Kosutzky, J.; Adamec, O.; Ledec, M.; Bobakova, E. 1975. **The effect of DDT on immunological reactivity in poultry.** *Environmental Quality and Safety Supplement* 3:573-576.

DDT (10 and 100 mg/kg; orally, for 14 days) had no significant effect on the antibody response to sheep red blood cells in hens and ducks and to human serum albumin in chickens. Immunoglobulin levels were unchanged.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

CHICKENS; DUCKS

104
Krivanek, N.; Reeves, A. L. 1972. **The effect of chemical forms of beryllium on the production of the immunologic response.** *American Industrial Hygiene Association Journal* 33(1):45-52.

Skin sensitivity to Be compounds, such as beryllium sulfate, beryllium guinea pig serum albuminate, beryllium hydrogen citrate, and beryllium aurintricarboxylate, involved an immunological reaction of the delayed type. In guinea pigs sensitized with BeSO4, beryllium hydrogen citrate and beryllium aurintricarboxylate produced negative immunological reactions, while the remaining two combinations elicited positive responses. Beryllium albuminate produced consistently stronger positive reactions than BeSO4, indicating that it contained an antigenic principle stronger than the hapten present in BeSO4.

Beryllium

GUINEA PIGS

105
Kuchuk, A. A. 1977. **Immunological response of superphosphate production workers with symptoms of respiratory tract pathology.** *Vrachebnoe Delo* 3:119-122 (RUS).

Of the workers, 36.2% showed a blastic transformation of lymphocytes, 31.2% a reduction in spontaneous rosette formation, and 34.4% a reduction of osmoticunstable lymphocytes. The decrease of the immunological reactivity occurred due to reduction of immunocompetent T-lymphocytes.

Superphosphate

HUMAN STUDIES

106
Latimer, J. W.; Siegel, H. S. 1974. **Immune response in broilers fed technical grade DDT. (Antibodies)** *Poultry Science* 53(3):1078-1083.

Four-week-old chicks were fed mash containing 625 ppm or less DDT and were inoculated intravenously at six weeks of age with killed Salmonella pullorum (SP) or a purified bovine serum albumin (BSA) antigen. SP and BSA antibody titers were determined on sera collected every 48 hr for two weeks or every 72 hr for three weeks, respectively. The ingestion of technical DDT did not consistently influence the antibody titers to SP or BSA of the chickens. The only difference occurred on the sixth day after inoculation, when SP titers were higher in birds receiving 50 ppm DDT than in those receiving 0 or 500 ppm DDT. Four-week-old chicks fed 2700 ppm DDT all died within 12 days after starting on the treated feed. Birds fed 900 ppm DDT showed symptoms of toxicity but not a difference in antibody response to SP antigen.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

CHICKENS

107
LaVia, M. F.; LaVia, D. S. 1979. **Phenol derivatives are immunosuppressive in mice.** *Drug and Chemical Toxicology* 2(1/2):167-177.

Mice housed in cages washed with a compound containing three phenol derivatives (o-phenylphenol, o-benzyl-p-chlorophenol, p-tert-amylphenol) showed an impairment of the ability to generate a plaque-forming cell response to sheep red blood cells. In mice fed the most abundant phenol derivative, o-phenylphenol, significant immunodepression was also observed. These data confirm earlier results of the immunodepressive effects of phenol derivatives in the B-cell response.

p-tert-Amylphenol; Phenol, 4-(1,1-dimethylpropyl)-; o-Phenylphenol; (1,1'-Biphenyl)-2-ol; o-Benzyl-p-chlorophenol; Phenol, 4-chloro-2-(phenylmethyl)-

MICE

108
Levine, S.; Sowinski, R. 1977. **T-lymphocyte depletion and lesions of choroid plexus and kidney induced by tertiary amines in rats.** *Toxicology and Applied Pharmacology* 40(1):147-159.

Four piperazine and seven piperidine derivatives caused depletion of T-lymphocytes in rat spleen and/or lymph node in one day similar to that produced by tilorone and its analogs. The piperazines and piperidines have little in common with tilorone and its analogs except that all are tertiary amines. The piperazine and piperidine derivatives were less potent than tilorone for T-cell depletion, but most of them had the additional effect of injuring the choroid plexus, some had the latter effect but not the former. Some of the smaller tilorone analogs also had both types of action. Among numerous tertiary amines used as drugs, a few quinolone and acridine antimalarials had similar actions. These studies revealed previously unknown pharmacological relationships between lymphocytes and the choroid plexus and between the kidney and choroid plexus. The former is important because of the potential therapeutic usefulness of tilorone as an immunoregulator. The latter is of interest because of similarities in function between renal tubules and the choroid plexus.

Piperidine; Piperazine; Tilorone

109
Levis, W. R.; Whalen, J. J.; Powell, J. A. 1975. **Studies on the contact sensitization of man with simple chemicals: III. Quantitative relationships between lymphocyte transformation, skin sensitivity, and lymphokine activity in response to dinitrochlorobenzene.** *Journal of Investigative Dermatology* 64(2):100-104.

Dinitrochlorobenzene (DNCB) coupled to peripheral blood erythrocytes or leukocytes forms a particulate complex, DNCB-antigen. The addition of DNCB-antigen induced blastogenesis and DNA synthesis in leukocyte cultures from DNCB-sensitized human subjects and not in leukocyte cultures from nonsensitized controls. In general, sensitized subjects who displayed a higher degree of cutaneous reactivity to DNCB, as manifested by duration and intensity of dermatitis, also showed a greater blastogenic response to DNCB-antigen in vitro. This quantitative correlation was not invariant. Certain soluble factor(s) or lymphokines are released following the addition of DNCB-antigen to leukocyte cultures prepared from some sensitive subjects who were rechallenged one or more times with DNCB. These lymphokines induce blastogenesis in secondary target leukocyte populations from nonsensitized subjects. Extended studies are presented which show little or no lymphokine activity in peripheral blood leukocyte cultures during a primary immune response, despite high degree of blastogenic activity in response to DNCB-antigen. Significant lymphokine activity was observed only following additional rechallenge with DNCB. Blastogenesis and skin reactivity specific for DNCB developed about the same time during a primary immune response. This, along with the quantitative correlation shown in this communication, suggests that both processes probably reflect thymic-dependent cellular immunity. The appearance of lymphokine activity following rechallenge with DNCB suggests that DNCB-induced lymphokines may represent an amplifying mechanism of the cellular immune response that involves recruitment of previously uncommitted lymphocytes.

Dinitrochlorobenzene; Benzene, chlorodinitro-

HUMAN STUDIES

110
Ljaljevic, J. 1977. **State of cellular immunity in nitrogen industry workers tested in Pancevo.** *Glas Srpska Akademija Nauka i Umetnostii Odeljenje Medicinskih Nauka* 29:71-75.

Of the 67 workers examined at the nitrogen plant, the deficiency of cellular immunity was shown in 14. This value is somewhat higher than that indicated in a general population (range 15 to 18%).

Nitrogen

HUMAN STUDIES

111
Loose, L. D.; Pittman, K. A.; Benitz, K. F.; Silkworth, J. B.; Mueller, W.; Coulston, F. 1978. **Environmental chemical-induced immune dysfunction.** *Ecotoxicology and Environmental Safety* 2(2):173-198.

Antibody formation, endotoxin sensitivity, and resistance to a challenge malarial infection were evaluated in mice fed a diet containing Aroclor 1242 or hexachlorobenzene. Antibody synthesis to the sheep red blood cells (SRBC) was significantly depressed in the treated (167 ppm) animals as evidenced by the fact that control mice elicited about a two-fold increase in antibody formation over the treated mice. Serum IgA concentrations in Arochlor 1242- and hexachlorobenzene-treated mice were consistently 40-80 mg/dL lower than control values. Gram-negative endotoxin sensitivity in Aroclor 1242- and hexachlorobenzene-treated mice was increased 5.2- and 32-fold, respectively, following dietary administration of 167 ppm of Aroclor 1242 or hexachlorobenzene for six weeks. An endotoxin hypersusceptibility was also noted three weeks after dietary administration. Decreased resistance to a malaria challenge was also demonstrated in the xenobiotic-treated mice. A 20% decrease of mean survival time of mice fed Aroclor 1242 for three or six weeks and inoculated with Plasmodium berghei was observed. Infected mice which had received hexachlorobenzene for three or six weeks manifested reductions in mean survival time of 24% and 31%, respectively. Thus, environmental contaminants impair host resistance and, since no concomitant histopathological alterations were observed in the treated mice, the evaluation of immune parameters may possibly be a sensitive indicator of toxicity.

Polychlorobiphenyl compounds; Hexachlorobenzene

MICE

112
Loose, L. D.; Pittman, K. A.; Benitz, K. F.; Silkworth, J. B. 1977. **Polychlorinated biphenyl- and hexachlorobenzene-induced humoral immunosuppression.** *RES Journal of the Reticuloendothelial Society* 22(3):255.

The effect of dietary administration of polychlorinated biphenyls (Aroclor 1242) and hexachlorobenzene on antibody production and Ig concentrations was evaluated. Aroclor 1242 or hexachlorobenzene administered at 167 ppm in the diet to male mice for six weeks resulted in a greater than two-fold decrease in peak primary splenic Ab PFC (plaque-forming cell) response to SRBC (sheep erythrocyte) antigen. A concomitant decrease in serum Igs was demonstrated in Aroclor-treated and in hexachlorobenzene-treated animals. Mice maintained on the diet containing 167 ppm of Aroclor 1242 or hexachlorobenzene and injected with a secondary challenge of SRBC two weeks following the primary immunization manifested a significant decrease in the secondary splenic Ab PFC response. No significant increase in tissue chemical levels occurred between 6 and 8.5 weeks in the lung, thymus, spleen, and serum, but the liver content of Aroclor 1242 and hexachlorobenzene increased. Histopathological examinations revealed no changes in the lung, thymus, mesenteric lymph nodes, and spleen; however, a significant and consistent hepatomegaly was observed.

Polychlorobiphenyl compounds; Hexachlorobenzene

MICE

113
Loose, L. D.; Silkworth, J. B.; Coulston, F. 1977. **Impaired host-defense in mice fed Aroclor 1242 or hexachlorobenzene for six weeks.** *Toxicology and Applied Pharmacology* 41(1):203

Impaired humoral immune response to sheep erythrocytes in mice fed 167 ppm PCB or HCB for six weeks has been suggested to be a result of macrophage dysfunction. Results of studies initiated to determine the extent of the PCB- and HCB-induced macrophage dysfunction relative to macrophage-mediated impaired host defense are presented. Male Balb/c mice were fed diets containing 167 ppm Aroclor 1242 or hexachlorobenzene for six weeks and sensitivity of the treated animals to gram-negative endotoxin was evaluated. Endotoxin suspended in saline was administered intraperitoneally and mortality recorded at 24 hr. The LD50 for endotoxin in controls was 1,000 micrograms, whereas HCB-treated mice had an LD50 of 50 micrograms, and mice fed 167 ppm PCB for six weeks showed an LD50 of 200 micrograms. A similar increase in sensitivity to the lethal effects of Plasmodium berghei infection was noted in these mice; mice inoculated with the malarial parasite showed an enhanced peripheral blood parasitemia and about a 50% reduction in mean survival time. Enhanced sensitivity to the lethal effects of endotoxin and the malarial parasite suggest a significantly impaired host-defense in animals exposed to environmental chemicals.

Polychlorobiphenyl compounds; Hexachlorobenzene

MICE

114
Loose, L. D.; Silkworth, J. B.; Mudzinski, S. P.; Pittman, K. A.; Benitz, K. F.; Mueller, W. 1979. **Modification of the immune response by organochlorine xenobiotics.** *Drug and Chemical Toxicology* 2(1/2):111-132.

Immune responses, including antibody formation, endotoxin sensitivity, and resistance to a challenge malarial infection, were measured in mice fed diets containing hexachlorobenzene (HCB) or Aroclor 1242, a polychlorinated biphenyl. A greater than 2X reduction in antibody formation to sheep red blood cells was noted in animals fed 167 ppm Aroclor 1242 or HCB in the diet. In addition, increased sensitivity to a gram-negative endotoxin (Salmonella typhosa) was observed in animals fed 167 ppm PCB or HCB. Decreased resistance to a malaria challenge was also demonstrated.

Polychlorobiphenyl compounds; Hexachlorobenzene

MICE

115
Loose, L. D.; Silkworth, J. B.; Pittman, K. A.; Benitz, K. F.; Mueller, W. 1978. **Impaired host resistance to endotoxin and malaria in polychlorinated biphenyl- and hexachlorobenzene-treated mice.** *Infection and Immunity* 20(1):30-35.

The in vivo effect of polychlorinated biphenyl (PCB) and hexachlorobenzene (HCB) on the sensitivity of mice to endotoxin and resistance to malaria is reported. Dietary administration of 167 ppm PCB 1242 or HCB for three weeks resulted in an enhanced sensitivity to gram-negative endotoxin. This was further increased in animals which remained on the diet for six weeks. A 20% decrease in mean survival time was seen in mice fed PCB 1242 for three or six weeks and inoculated with malaria; infected mice receiving HCB for three or six weeks showed a reduction in mean survival time of 24% or 31%, respectively. Centrilobular and pericentral hepatocyte hypertrophy, common following exposure to organochlorines, was noted; however, normal thymus, lungs, spleen, and mesenteric lymph nodes were seen following histopathological examination. Significant deposits of the xenobiotics were observed following electron capture gas chromatography analysis for PCB and HCB. Results indicate that environmental chemicals impair host resistance; possibly this alteration is related to the presence of these chemicals in the lymphoreticular organs.

Hexachlorobenzene; Polychlorobiphenyl compounds

MICE

116
Luster, M. I.; Faith, R. E.; Lawson, L. D. 1979. **Effects of 2,3,7,8-tetrachlorodibenzofuran (TCDF) on the immune system in guinea pigs.** *Drug and Chemical Toxicology* 2(1/2):49-60.

The effects of 2,3,7,8-tetrachlorodibenzofuran (TCDF) exposure on cell-mediated and humoral immune functions in Hartley guinea pigs were investigated. TCDF was administered by gavage at doses of 0.05, 0.17, 0.5, and 1.0 micro-g/kg body weight weekly for six weeks. TCDF modestly suppressed cell-mediated immune function and had slight effects on humoral immunity. This study suggests that immune effects caused by TCDF are similar to that reported by TCDD in adult guinea pigs.

TCDF, 2,3,7,8-

GUINEA PIGS

117
Luster, M. I.; Faith, R. E.; Moore, J. A. 1978. **Effects of polybrominated biphenyls (PBB) on immune response in rodents.** *Environmental Health Perspectives* 23:227-232.

Mice and rats received 22 daily treatments of 0.03, 0.3, 3.0, or 30 mg FireMaster FF 1/kg in a period covering 30 days. Exposure severely depressed cell-mediated immunity in both mice and rats at the higher dosage levels as indicated by depressed responsiveness of splenic lymphocytes to mitogenic stimulation by polyclonal T-cell activators. Humoral immunity was depressed in mice at the 30 ppm dosage level. Assays for humoral immune functions included antibody production, serum Ig levels, and mitogenic stimulation of splenic lymphocytes to a polyclonal B-cell activator. Thus, FireMaster FF 1 exposure can lead to suppression of humoral and particularly cell-mediated immune responses.

Polybromobiphenyl compounds

MICE; RATS; HUMAN STUDIES

118
Maibach, H. I.; Johnson, H. L. 1975. **Contact urticaria syndrome: contact urticaria to diethyltoluamide (immediate-type hypersensitivity).** *Archives of Dermatology* 111(6):726-730.

Contact urticaria refers to a wheal-and-flare response occurring on the application of chemicals to intact skin. Observations should be made using open patch tests 15 to 30 min after application. The syndrome can be divided into three subdivisions: nonimmunologic cause, immunologic cause, and uncertain cause. This patient had contact urticaria due to the insect repellent, diethyltoluamide. This case was probably due to an immunologic response (immediate hypersensitivity) and the specificity of response was demarcated. Immunologically mediated cases cover a broad range of manifestations from contact urticaria only to local urticaria plus asthma and, in extreme sensitivity, anaphylactic responses.

Diethyltoluamide; Benzamide, N,N-diethylmethyl-

HUMAN STUDIES

119
Maier, A.; Batzenschlager, A.; Orion, B. 1974. **Allergic pulmonary thromboarteriopathy in the course of occupational inhalation of organic dust.** *Archives des Maladies Professionnelles* 35(10/11):875-892 (FRE).

Analysis of clinical, histopathological, functional, and immunological data from patients suffering from occupational or paraoccupational pneumopathies with precipitins results in a broad variety with arterial lesions predominating. These vascular lesions seem to come within the scope of the deteriorations following the formation of immune endovascular complexes characteristic of Coombs Type III allergic reactions. It is important that exposures to exogenous aggressions of an organic nature be considered in cases such as these.

HUMAN STUDIES

120
Miller, K. 1979. **Alterations in the surface-related phenomena of alveolar macrophages following inhalation of crocidolite asbestos and quartz dusts: an overview.** *Environmental Research* 20(1):162-182.

Rats were exposed to quartz and asbestos dusts by inhalation to provide a model of the in vivo participation of the constituent mononuclear phagocytes. Early changes included alteration of macrophage surface morphology and an increased number of IgG receptor sites. In vivo membrane deposition of complement components on alveolar macrophages from crocidolite-dusted rats was demonstrated. A prolonged physical interaction followed by lymphocyte proliferation occurred when macrophages from crocidolite-dusted rats were cultured in vitro with splenic lymphocytes. The surface alterations leading to these phenomena were characterized. Dusted macrophages possibly participate in both cell-mediated and humoral interactions, and host factors may contribute to the development of dust diseases.

Asbestos; Quartz

RATS

121
Miller, K.; Kagan, E. 1977. **Immune adherence reactivity of rat alveolar macrophages following inhalation of crocidolite asbestos.** *Clinical and Experimental Immunology* 29(1):152-158.

Immune adherence was used to show in vivo deposition of complement on membranes of alveolar macrophages from rats chronically exposed to crocidolite asbestos dust. Pre-treatment of macrophage cultures with anti-C3 antiserum greatly diminished the level of immune adherence reactivity. In vitro exposure of alveolar macrophages to crocidolite asbestos did not result in significant levels of immune adherence reactivity. These results may reflect an in vivo antigen-antibody-complement interaction on the surface of alveolar macrophages from animals which have inhaled asbestos dust.

Asbestos

RATS

122
Miller, S. D.; Zarkower, A. 1974. **Alterations of murine immunologic responses after silica dust inhalation.** *Journal of Immunology* 113(5):1533-1543.

Inhalation of silica dust by mice enhanced the transformation of concanavalin A-responsive T-lymphocytes in the spleen and decreased response in the cells of the mediastinal lymph nodes (MLN). Mice exposed to silica dust for two weeks before and three weeks after aerosol or subcutaneous immunization with Mycobacterium tuberculosis H37Ra exhibited enhanced uptake of 3H-thymidine upon culture of their spleen lymphocytes with purified protein derivatives of tuberculin. The lipopolysaccharide-responsive B-lymphocytes of both spleen and MLN culture exhibited decreased uptake of 3H-thymidine. The

treated animals also had lower numbers of plaque-forming cells (PFC) in the spleen, decreased serum agglutinin activity, and lower numbers of PFC in the MLN when assayed with Escherichia coli LPS-coated sheep red blood cells after aerosol immunization with whole E. coli O55:B5. The possible nature of the immunological alterations induced by silica dust is discussed.

Silica

RATS; MICE

123
Misiewicz, A. 1979. **Immunoelectrophoretic pattern of serum in humans exposed to atmospheric pollutants emitted by artificial fertilizer plants.** *Wiadomosci Lekarskie (Poland)* 32(16):1125-1130 (POL).

HUMAN STUDIES

124
Moore, J. A. 1979. **The immunotoxicology phenomenon (polychlorinated biphenyls, halogenated hydrocarbons).** *Drug and Chemical Toxicology* 2(1/2):1-4.

Polychlorobiphenyl compounds

125
Moore, J. A.; Faith, R. E. 1976. **Immunologic response and factors affecting its assessment.** *Environmental Health Perspectives* 18:125-131.

The potential harmful effects of toxic compounds on the developing immune system are discussed. This discussion is illustrated by results of studies on the effects of 2,3,7,8,-tetrachlorodibenzo-p-dioxin on the developing immune system of Fischer rats. While this compound and several others have been shown to have immunosuppressive effects, the available data do not support routine evaluation of the consequence of chemical exposure to the developing immune system.

TCDD, 2,3,7,8-

RATS

126
Moore, J. A.; Luster, M. I.; Gupta, B. N. 1978. **Toxicological and immunological effects of a commercial polybrominated biphenyl mixture (Firemaster FF-1).** *Toxicology and Applied Pharmacology* 45(1):295-296.

F-344 rats and B6C3F1 mice received up to 22 doses of Firemaster FF-1 by gavage (0, 0.03, 0.3, or 30 mg/kg/day, five days/week) and were sacrificed at 15, 31, 46, and 64 days. Male mice and rats lost body weight at the highest dose; rat weight loss was significant after eight doses and persisted throughout the study. Hepatocellular swelling, liver weight increases, and increased lipid deposition occurred in rats and mice receiving 3.0 and 30 mg/kg. At the two higher doses, splenic lymphocytes were less responsive to the T-cell mitogens phytohemagglutin and concanavalin A. The 30 mg/kg dose depressed mice response to lipopolysaccharide, a B-cell mitogen. Serum immunoglobulin G levels decreased in mice treated with 30 mg/kg; no differences were detected in the immunoglobulins M and A.

Polybromobiphenyl compounds

RATS; MICE

127
Moore, J. A.; Zinkl, J. G.; Vos, J. G. 1973. **Effect of TCDD on immune system of lab animals.** *Environmental Health Perspectives* 5:149-165.

To test cell-mediated and humoral immunity, groups of guinea pigs were dosed weekly for eight weeks with TCDD (0, 0.008, 0.04, 0.2, or 1 micro-g/kg body weight). All animals at the 1 micro-g/kg level died or were killed when moribund. They showed severe weight loss, lymphopenia, and lymphoid organ atrophy. Cell-mediated immunity was assessed by vaccination of the remaining animals with an oil suspension of killed Mycobacterium tuberculosis. Thymus atrophy and lymphopenia were observed. At the 0.2 and 0.04 micro-g/kg dosages, diameters of the skin reaction were significantly reduced when measured 24 and 48 hr following tuberculin treatment. In a second experiment, humoral immunity was stimulated by tetanus toxoid injections. Serum tetanus antitoxin concentrations were slightly depressed in the 0.2 micro-g/kg level on days 49 and 56. In a skin test done in rats, animals treated with 5.0 micro-g/kg had significantly lower body, thymus, and adrenal weights, although no effect was noted in skin reactions. Cell-mediated immunity was tested in mice in a graft-versus-host assay. Weights of draining popliteal lymph nodes were significantly lower in animals injected with spleen cells from animals treated with 5 micro-g/kg group. It was concluded that TCDD at sublethal doses slightly suppresses humoral immunity in the guinea pig, while cell-mediated immunity is suppressed in both guinea pigs and mice.

TCDD, 2,3,7,8-

GUINEA PIGS; RATS; MICE

128
Moszczynski, P. 1979. **Evaluation of the total immunity of workers exposed to organic solvents containing benzene and its homologues.** *Medycyna Pracy (Poland)* 30(3):225-229 (POL).

Workers exposed to benzene, toluene, and xylene at concentrations up to 370, 580, and 506 mg/cu m of air, respectively, showed an increase in acidic phosphatase and beta-glucuronidase activities in neutrophiles, a decrease in intracellular glycogen, and a reduction in the number of T-lymphocytes. In some workers, urinary phenol and hippuric acid exceeded 16 and 900 mg/L, respectively.

Benzene; Toluene; Benzene, methyl-; Xylene; Benzene, dimethyl-

HUMAN STUDIES

129
Mueller, S.; Gillert, K. E.; Krause, C.; Gross, U.; Age-Stehr, J. L.; Diamantstein, T. 1977. **Suppression of delayed-type hypersensitivity of mice by lead.** *Experientia (Basel)* 33(5):667-668.

Application of Pb as Pb(OAc)2 suppressed the delayed-type hypersensitivity (DTH) of mice induced by sheep red blood cells. Inhibition of elicitation of DTH in primary as well as in secondary response was correlated with the concentration of Pb in the blood of the mice.

Lead

MICE

130
Mueller, S.; Gillert, K. E.; Krause, C.; Jautzke, G.; Gross, U.; Diamantstein, T. 1979. **Effects of cadmium on the immune system of mice.** *Experientia (Basel)* 35:909.

Cadmium in the form of cadmium acetate was administered to mice ad libidum with drinking water for ten weeks to test the effects of Cd(2+) on the immune system of these animals. Groups of Cd(2+)-treated and control mice were sensitized with sheep red blood cells (SRBC), challenged by a single intracutaneous footpad injection of the antigen to provoke a specific delayed-type hypersensitivity reaction (DTH), and intensity of the reaction measured by footpad swelling due to the inflammatory response. DTH reactions were inhibited in animals fed Cd(2+); inhibition was related with the concentration detected in the serum. To examine the effect of Cd(2+) on the humoral response, groups of test and control animals were injected intraperitoneally with SRBC following immunization with these cells and the number of IgM and IgG antibody-forming cells in the spleen determined using the plaque assay of Cunningham and Szenberg. Mice treated with doses as low as 600 ppm Cd(2+) showed no significant reduction in anti-SRBC-plaque-forming spleen cells. In addition, spleen cells derived from mice fed Cd(2+) showed in vitro enhanced response to T- and B-cell mitogens. These results show that Cd(2+) exposure alters the immune systems of mice.

Cadmium

MICE

131
Munson, A. E. 1979. **Development of short-term immunotoxicological assays for the prediction of chronic toxicological response induced by environmental chemicals.** *U.S. NTIS Report* AD-A080636, 170 pp.; AD-A080621, 169 pp.

The overall goal of the research is to systematically develop a battery of in vitro physical, biochemical, and functional assays to predict subchronic or chronic toxicologic behavior that would be produced by in vivo exposure to a chemical. The general experimental plan utilizes both in vivo and in vitro approaches. Mice were exposed subchronically to trichloroethylene (TCE-2), and studies performed to assess bone marrow status, cell-mediated immunity, humoral immunity, macrophage function, and standard toxicologic parameters. An in vitro, tier assay system is being developed which includes two cytotoxicity tests, assessment of DNA synthesis, phagocytosis, lymphocyte responsiveness to mitogens, enumeration of bone marrow stem cells, and an antibody-forming cell assay. The LD50's for male and female mice exposed by the gastrointestinal tract to TCE-2 were 2402 and 2454 mg/kg, respectively. In a combination range-finding study of TCE-2 in the drinking water and 30-day interaction with emulphor (1%), there were only four parameters significantly different from the appropriate control, but none of these parameters showed dose dependency and could not be specifically attributed to an interaction between TCE-2 and emulphor.

Trichloroethylene; Ethene, trichloro-

MICE

132
Munson, A. E.; Sanders, V. M.; Borzelleca, J. F. 1978. **Reticuloendothelial system function in mice exposed to four haloalkanes: drinking water contaminants.** *Toxicology and Applied Pharmacology* 45(1):329-330.

The functional activity of the mouse reticuloendothelial system, as indicated by the phagocytic index (p.i.) and organ distribution of 125I-labeled Listeria monocytogenes, was monitored after a 90-day gastric-gavage administration of chloroform (CHCl3), bromodichloromethane (CHBrCl2), bromoform (CHBr3), or dibromochloromethane (CHBr2Cl). None of the haloalkanes affected the p.i. Chloroform doses of 50 and 150 mg/kg, respectively, decreased the liver uptake of Listera 9% and 24% in female mice; males exhibited a dose-dependent decrease in hepatic phagocytosis but no changes in splenic or pulmonary localization. Hepatic phagocytosis was suppressed in males and females by bromodichloromethane (45% and 18%, respectively, at the highest dose), bromoform (28% and 53%, respectively, at the highest dose), and dibromochloromethane. All other reticuloendothelial parameters were within normal ranges.

Chloroform; Methane, trichloro-; Bromodichloromethane; Methane, bromodichloro-; Dibromochloromethane; Methane, dibromochloro-; Bromoform; Methane, tribromo-

MICE

133
Nehlsen, S. L.; Lalezari, P. 1977. **Suppression of T-cell-mediated immune responses by sodium cyanate.** *Transplantation Proceedings* 9(1):997-1000.

NaCNO-induced sub-neurotoxic immunosuppression was examined in vivo, in adult CBA mice. Results showed increased survival of skin allograft and reduced lymph node response to oxazolone skin printing in mice treated daily with 0.1-3.3 mg cyanate. Thus, NaOCN may inhibit thymus lymphocyte recognition of antigens.

Sodium cyanate

MICE

134
Ohi, G.; Fukuda, M.; Seto, H.; Yagyu, H. 1976. **Effect of methylmercury on humoral immune responses in mice under conditions simulated to practical situations.** *Bulletin of Environmental Contamination and Toxicology* 15(2):175-180.

The effect of methylmercury on humoral immune mechanisms in mice dosed with relatively large amounts of methylmercury for a short period, fed relatively low levels subchronically as adults, or exposed from very early stages of life until sexual maturity are described. When relatively large doses of methylmercury were administered over a short time period, a suppression and delay in reaching the peak of primary humoral response was noted in these animals.

Methylmercury

MICE

135
Oishi, S.; Hiraga, K. 1980. **Effect of polychlorinated biphenyl, dibenzofuran, and dibenzo-p-dioxin on the susceptibility of male mice to endotoxin.** *Journal of Environmental Science and Health. Part B. Pesticides, Food Contaminants, and Agricultural Wastes* B15(1):77-85.

The effect of PCB, dibenzo-p-dioxin (CDD), and dibenzofuran (CDF) on endotoxin sensitivity was studied in male mice. The oral administration of CDF and CDD weekly for four weeks increased endotoxin sensitivity; PCB was not effective. On the other hand, residual levels of PCB were detected in thymus, but CDF and CDD were not.

Polychlorobiphenyl compounds; Chlorodibenzofuran; Chlorodibenzodioxin

MICE

136
Olefir, A. I. 1978. **Immunological reactivity of the progeny of animals affected by pesticides.** *Gigiena i Sanitariya* (2):103-104 (RUS).

Repeated exposure of pregnant rats to small concentrations (1% LD50) of chlorofos and Yalan in air decreased the activity of nonspecific factors of immunity, the protective properties of the skin and mucus, and the resistance to infection among the first-generation offspring. The activity of the reticuloendothelial system remained unchanged.

Chlorophos; Phosphonic acid, (2,2,2-trichloro-1-hydroxyethyl)-, dimethyl ester; Yalan; 1H-Azepine-1-carbothioic acid, hexahydro-, S-ethyl ester

RATS

137
Olefir, A. I. 1974. **Effect of chemical substances on the formation of acquired immunity.** *U.S. NTIS Report* AD-A008261, 9 pp.

An experimental study is presented on the effects of carbamate pesticides, chlorophos, and DDT on the dynamics of formation of anti-typhus abdominalis agglutinins in rats and protective properties of rat serum in mice.

Carbamates; Chlorophos; Phosphonic acid, (2,2,2-trichloro-1-hydroxyethyl)-, dimethyl ester; DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

RATS

138
Olefir, A. I.; Mintser, O. P. 1977. **Relation of natural resistance disorders to the effect of pesticides.** *Vrachebnoe Delo* 9:121-123 (RUS).

An inverse proportional dependence was observed between the intensity of action of pesticides in rats and the complement activity of blood serum. The pesticides were administered at 1/1000-1/20 LD50. Sevin and Yalan inhibited the bactericidal activity of serum only at toxic (1/20 LD50) doses, while all the other pesticides tested did not affect the bactericidal activity of serum at either low or toxic doses.

Pesticides; Carbaryl; 1-Naphthalenol, methylcarbamate; Yalan; 1H-Azepine-1-carbothioic acid, hexahydro-, S-ethyl ester

RATS

139
Olefir, A. I.; Mintser, O. P.; Sova, R. E. 1977. **Interrelation of indexes of natural body resistance during chronic poisoning with chlorophos, polychloropinene, and Sevin.** *Gigiena i Sanitariya* (4):25-28 (RUS).

Rats were orally administered Sevin, polychloropinene, or chlorophos for 4.5 months at 1/20 LD50, and immunological and body resistance parameters such as serum complement activity, lysosyme and beta-lysine levels, in vivo absorptive and digestive activity of neutrophils with respect to staphylococci, and skin bactericidal capacity and Escherichia coli contamination. The parameters were useful in assessing the terms and durations of various stages of the adaptive process or predominance of toxic action.

Carbaryl; 1-Naphthalenol, methylcarbamate; Chlorophos; Phosphonic acid, (2,2,2-trichloro-1-hydroxyethyl)-, dimethyl ester; Polychloropinene

RATS

140
Olsen, R. G. 1980. **Immune dysfunctions and abrogation of the inflammatory response by environmental chemicals.** Research at Ohio State University, Department of Medicine, Columbus OH; Sponsored by U.S. Dep. of Defense, Washington DC, code DF056030; 7/79-8/80.

The Air Force uses large amounts of high-energy fuels and chemicals in its normal operations. In order to protect personnel and the environment, the Air Force is required to assess the biological effects of these compounds. Additional information on the sublethal effects of toxicants is required for an accurate assessment of their potential harmful effects. No information is available on the effects of AF chemicals on immune-response systems. The objective of this research is to determine the sublethal effects of AF-utilized chemicals on the immune system of animals. This work will provide information necessary to evaluate the effects of AF chemicals on the basic immune responses of organisms. Using Swiss mice, potentially immunosuppressive compounds will be evaluated for their ability to suppress in vivo immunologic functions. Purified lymphocytes from treated animals will be assayed for suppression by in vitro assays. These procedures will establish which compounds induce immunosuppression and determine whether the in vitro assays are reliable correlates of chemically induced energy. Compounds to be tested include hydrazine analogues, naphthylamines, and benzo(a)pyrene.

Hydrazine; Naphthylamines; Benzo(a)pyrene

MICE

141
Osebold, J. W.; Owens, S. L.; Chung-Zee, Y. 1979. **Immunological alterations in the lungs of mice following ozone exposure: changes in immunoglobulin levels and antibody-containing cells.** *Archives of Environmental Health* 34(4):258-265.

Specific pathogen-free mice were placed in environmental chambers containing ozone. At levels of 0.5 and 0.8 ppm, the oxidant was seen to have inflammatory effects as shown by rising serum albumin levels in lung lavage fluid. Fluorescein conjugated anti-heavy chain sera were used to detect cells containing IgM, IgG, and IgA in measured lung areas termed Pulmonary Units. Antigenic stimuli occurred along the airways, with significant increases of IgA-containing cells in the bronchus-associated lymphoid tissue. No increase in the numbers of IgM- and IgG-containing cells was noted. Immunodiffusion analyses for immunoglobulins in lung lavage fluid indicated increases of IgG1, IgG2, and IgA in lung secretions. The calculation of changing Ig/Alb ratios suggested that the IgA present was largely the result of local synthesis, while IgG molecules were mainly of serum origin. Possible sources of the antigenic stimuli to ozone-exposed lungs are discussed.

Ozone

MICE

142
Parker, C. W. 1977. **Immune responses to environmental antigens absorbed through the gastrointestinal tract.** *Federation Proceedings* 36(5):1732-1735.

143
Patterson, R.; Addington, W.; Banner, A. S. 1979. **Antihapten antibodies in workers exposed to trimellitic anhydride fumes: a potential immunopathogenetic mechanism for the trimellitic anhydride pulmonary disease-anemia syndrome.** *American Review of Respiratory Disease* 120(6):1259-1267.

The pulmonary disease-anemia syndrome which occurs following inhalation of trimellitic anhydride (TMA) consists of cough, hemoptysis, and dyspnea with pulmonary infiltrates, a restrictive respiratory defect, anemia, and hypoxemia. The disease varies in severity, and a possible fatal case has been identified. Although previously considered a chemical pneumonitis, the recognition of two other types of immunologically mediated TMA inhalational diseases prompted analysis of serum antibodies in six workers with TMA pulmonary disease-anemia syndrome and six co-workers of the most severely ill subject. A comparison was made with antibody concentrations of TMA workers previously identified as having other respiratory syndromes due to the inhalation of TMA powder in the production plant. Trimellityl human serum albumin and trimellityl human erythrocytes were used as antigens. Workers with the TMA pulmonary disease-anemia syndrome had antibody concentrations comparable to those of workers with other types of immunologic TMA respiratory disease, but coworkers, who apparently were also exposed to TMA fumes, could not be distinguished clearly by these immunoassays. The inhalation of TMA appears to be a significant stimulus of a systemic immune response. The pathogenesis of the TMA-induced pulmonary disease-anemia syndrome may result from a complex interaction between the chemical toxicity of TMA fumes, the degree of exposure to TMA fumes of the individual worker, and an immune reaction against TM haptenized proteins and cells of the repiratory system.

Trimellitic anhydride; 5-Isobenzofurancarboxylic acid, 1,3-dihydro-1,3-dioxo-

HUMAN STUDIES

144
Pepys, J. 1974. **Immunologic approaches in pulmonary disease caused by inhaled materials.** *Annals of the New York Academy of Sciences* 221:27-37.

A review on respiratory tract reaction to inhaled organic and inorganic allergens and the role of demonstrable antibodies is presented.

145
Pepys, J. 1976. **Allergic respiratory disease due to inhaled chemical dusts and gases.** *Bulletin Europeen de Physiopathologie Respiratoire* 12(4):120-121.

146
Pepys, J. 1977. **Occupational respiratory allergic reactions to chemical dusts and gases.** *Excerpta Medica International Congress Series* 414:381-387.

147
Perelygin, V. M.; Shpirt, M. B.; Aripov, O. A.; Ershova, V. I. 1971. **Effect of some pesticides on immunological response reactivity.** *Gigiena i Sanitariya* (12):29-33.

TMTD (thiram), DDT, Sevin (0.1 mg/kg), and zineb (10 mg/kg) did not produce any stable changes in immunological reactivity in albino rats and rabbits. DDT, TMTD (0.5 mg/kg), zineb (100 mg/kg), and Sevin (20 mg/kg) produced decreases in antibody formation, phagocytic activity of leukocytes, and protective properties of serum. An increase in reactivity was noted at the beginning, followed by a decrease. Treatment with Sevin (200 mg/kg), DDT, TMTD (1 mg/kg), and zineb (500 mg/kg) caused a prolonged, gradual fall in reactivity. Shifts in immunological reactivity which develop following exposure to certain pesticides are an indication of clinical signs specific for pathological changes.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Carbaryl; 1-Naphthalenol, methylcarbamate; Thiram; Thioperoxydicarbonic diamide (((H2N)C(S))2S2), tetramethyl-; Zineb; Zinc, ((1,2-ethanediylbis(carbamodithioato))(2-))-

RATS; RABBITS

148
Perkins, E. H. **Chemical effects on the immune system.** Research at Oak Ridge National Laboratory, Biology Division, Oak Ridge TN; Sponsored by DOE, Washington DC, code 001560; 0/78-N/A.

Two approaches are under way: (1) to establish suitable technology for examining the effects of environmental compounds, including fossil fuel by-products and nuclear fuel components, on immune unresponsiveness in mice; and (2) to perform mechanism studies aimed toward clarifying the suspected role of depressed immune competence in chemical carcinogenesis. The recovery of the immune system from such injury will be assessed. Results will be published in the open literature.

149
Poberezkina, D. I.; Ivashina, S. A. 1978. **Effect of industrial contact with grizin on nonspecific immunity factors.** *Antibiotiki (Moscow)* 23(4):321-325.

Results from dynamic examination of persons occupationally exposed to grizin, an antibiotic used as a food additive, are presented. Contact with grizin resulted in changes in the humoral, cell, and barrier factors of the nonspecific immunity; these changes and their manifestations differed depending on the age, period, and contact level. The authors were able to detect changes in the state of the nonspecific immunological reactivity of exposed persons prior to the appearance of clinically pronounced forms of the pathology.

Grizin

HUMAN STUDIES

150
Prenner, B. M.; Stevens, J. J. 1976. **Anaphylaxis after ingestion of sodium bisulfite.** *Annals of Allergy* 37(3):180-182.

The occurrence of anaphylaxis is reported following ingestion of food sprayed with sodium bisulfite. In this instance the patient apparently formed specific IgE antibody, probably via a haptenic mechanism. This case report should alert physicians to consider food additives as well as the foods themselves when seeking agents responsible for such reactions.

Sodium bisulfite

HUMAN STUDIES

151
Rakhimova, M. T. 1977. **Nonspecific immunological reactivity characteristics and sickness rate among workers at a titanium magnesium combined plant.** *Gigiena Truda i Professional'nye Zabolevaniya* 21(10):29-32 (RUS).

Workers at a titanium-magnesium plant exposed to a number of chemicals including chlorine and its compounds showed changes in parameters of nonspecific immunity including falling phagocytic activity of the blood leukocytes due to disrupted capture phase and inhibition of the phagocytic and adsorption capacity of the buccal mucosa. Recommendations for raising the immunologic reactivity and reducing disease incidence rates are given.

Magnesium; Titanium; Chlorine

HUMAN STUDIES

152
Rao, D. S. V. S.; Glick, B. 1977. **Pesticide effects on the immune response and metabolic activity of chicken lymphocytes.** *Proceedings of the Society for Experimental Biology and Medicine* 154(1):27-29.

Immune response and metabolic activity of bursal, splenic, and thymic lymphocytes from chickens treated with DDT and mirex were evaluated. A marked reduction was observed in the metabolic activity upon pesticide treatment. There was no significant difference in total antibody production, but IgG levels were significantly reduced and IgM levels were markedly elevated. The significance of reduced metabolic activity and IgG production are discussed in relation to T-cell activity.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Mirex; 1,3,4-Metheno-1H-cyclobuta(cd)pentalene, 1,1a,2,2,3,3a,4,5,5,5a,5b,6-dodecachlorooctahydro-

CHICKENS

153
Reichrtova, E.; Takac, L. 1977. **Effect of magnesite dust exposure on immune mechanisms in rats.** *Environmental Pollution* 14(2):133-138.

The influence of industrial magnesite dust exposure on immune mechanisms was investigated in rats. The following determinations were made on control and treated animals: specific antibody production to antigen (sheep red blood cells), total serum complement, and lung autoantibody formation. Magnesite dust administered intravenously or intratracheally caused an increased number of hemolysin plaque-forming cells in spleen as well as in lung. Exposure of animals to magnesite dust in inhalation chambers for two months evoked the increase of total serum complement, whereas animals exposed for three months had titers of lung autoantibodies within the same range as the control group. Exposure to magnesite dust apparently induces a modification of immune processes.

Magnesite

RATS

154
Reigart, J. R.; Graber, C. D. 1976. **Evaluation of the humoral immune response of children with low level lead exposure.** *Bulletin of Environmental Contamination and Toxicology* 16(1):112-117.

Normal and lead-exposed children with evidence of metabolic impairment showed no significant differences in major immunoglobulins, total complement, the third component of complement, or the anamnestic response to tetanus toxoid. Although there was a tendency to low total complement in both groups, no significantly lower levels of either total complement or the third component of complement were evident in the lead-exposed children before or after toxoid immunization.

Lead

HUMAN STUDIES

155
Resnick, H.; Morgan, W. K. C. 1971. **Immunoglobulin levels in berylliosis.** *Inhaled Particles III,* ed. W. H. Walton, vols. I and II, pp. 589-597. Surrey, England: Unwin Brothers Ltd.

Beryllium

156
Roales, R. R.; Perlmutter, A. 1977. **The effects of sublethal doses of methylmercury and copper, applied singly and jointly, on the immune response of the blue gourami (Trichogaster trichopterus) to viral and bacterial antigens.** *Archives of Environmental Contamination and Toxicology* 5(3):325-331.

Exposure of blue gouramis to methylmercuric chloride, to copper, or to methylmercury plus copper decreased the immune response of the fish to infectious pancreatic necrosis virus and Proteus vulgaris. No interaction between these metals was shown with regard to this phenomenon. Apparently, sublethal doses of methylmercury or copper, jointly or singly, are capable of affecting fish in manners other than growth and reproduction.

Copper; Methylmercuric chloride; Chloromethylmercury

FISH

157
Robohm, R. A.; Nitkowski, M. F. 1974. **Physiological response of the cunner, Tautogolabrus adspersus, to cadmium. IV. Effects on the immune system.** *NOAA (National Oceanic and Atmospheric Administration) Technical Report NMFS (National Marine Fisheries Service) Circular* 681:15-20.

Cadmium (12 ppm CdCl2, exposed for 96 hr) increased clearance of intracardially injected bacteria from the blood stream in cunners. The bacterial uptake by phagocytes of the liver and spleen increased, but the rate of bacterial killing within these cells was decreased. Cadmium at 3 to 24 ppm failed to influence antibody formation against injected sheep red blood cells. Thus, cadmium affects cellular immunity but not humoral immunity.

Cadmium

FISH

158
Rossouw, D. J.; Engelbrecht, F. M. 1979. **The effect of paraquat on the aerobic metabolism of rabbit alveolar macrophages and lung fibroblasts.** *South African Medical Journal* 55(1):20-23.

In this study the effects of paraquat on the aerobic metabolism and viability of isolated rabbit alveolar macrophages and lung fibroblasts were compared with the effects of other known metabolic inhibitors, sodium fluoride (NaF) and potassium cyanide (KCN). The manometrically and polarographically

determined endogenous oxygen consumption of lavaged alveolar macrophages compared very well. Exogenous glucose and autologous serum added to the medium had no significant effect on the basal respiration rate. Like sodium fluoride (20mM) and potassium cyanide (5 mM), paraquat (2 mM) decreased the viability of the macrophages far less than it did the oxygen utilization of the viable cells and resulted in an 80% inhibition of oxygen uptake. In contrast, paraquat induced a marked stimulation (230%) of the cyanide-insensitive respiration of alveolar macrophages. The concentrations of paraquat (nmol/1000 cells) which reduce macrophage metabolism to almost zero were virtually non-toxic to fibroblasts, as measured by their oxygen consumption.

Paraquat; 4,4'-Bipyridinium, 1,1'-dimethyl-

RABBITS

159
Roszkowski, J.; Zadura, J. 1976. **The effect of lindane on immune response in chickens.** *Bulletin of the Veterinary Institute in Pulawy* 20(3/4):88-91.

Chickens treated with 50 mg lindane/kg one day before, on the day of, and one or three days after immunization with sheep red blood cells showed no significant differences in immunological indices. Chickens given lindane on the second day after immunization showed a decrease in hemolysin titer. Chickens treated with 20 mg/kg daily for 48 days had lowered immunological indices and absolute spleen weights; however, only the spleen weight differences were significant.

Lindane; Cyclohexane, 1,2,3,4,5,6-hexachloro-, (1alpha,2alpha,3beta,4alpha,5alpha,6beta)-

CHICKENS

160
Roszkowski, J.; Zadura, J.; Skwarek, P. 1976. **The effect of carbaryl on immune response in chickens.** *Bulletin of the Veterinary Institute in Pulawy* 20(3/4):85-88.

Chickens treated orally with 500 mg/carbaryl kg one day before; on the day of; or one, two, or three days after immunization with 1% sheep red blood cells showed inhibited hemolysin production and decreased numbers of splenic germinal centers. Hemagglutinin levels were not altered by the treatment.

Carbaryl; 1-Naphthalenol, methylcarbamate

CHICKENS

161
Rusakov, N. V.; Korotkova, G. I.; Bikbulatov, V. S. 1973. **Experimental study of the allergenic action of ortho- and para-nitrochlorobenzene.** *Gigiena i Sanitariya* (3):13-16.

Various benzene compounds occur as atmospheric contaminants. Ortho-nitrochlorobenzene (ONCB) and para-nitrochlorobenzene (PNCB) can be found in the air over populated places in quantities which exceed the permissible standard. Discharges from production of nitrochlorobenzene usually contain a complex of its isomers. Formed as a by-product during industrial preparation of ONCB and PNCB, 2,4-dinitrochlorobenzene possesses sharply expressed allergenic properties. Results of tests on the sensitization of animals to this compound are reported.

o-Chloronitrobenzene; Benzene, 1-chloro-2-nitro-; p-Chloronitrobenzene; Benzene, 1-chloro-4-nitro-; 2,4-Dinitrochlorobenzene; Benzene, 1-chloro-2,4-dinitro-

162
Sacher, G. A. **Early and late effects of energy-related pollutants on experimental animals-physiological and immunological measures in aging rodents.** Research at U.S. Department of Energy, Division of Biological and Medical Research, Argonne IL; Sponsored by DOE, Washington DC, code 000104; 0/78-N/A.

Indices of physiological response including temperature, muscular activity, and oxygen consumption to thermal stress and exposure to environmental pollutants are being monitored continuously and the data subjected to time series analysis. This phase of the study utilizes two mouse strains-Mus musculus and Peromyscus leucopus. Interesting facets of the latter are its cellular repair and protection systems and the closer array of spontaneous tumor types to those in man. Humoral and cell-mediated immunity and their response to carcinogenic pollutant exposure is being assayed in BCF/1 mice or cultured spleen cells by immunization with sheep red cells or mouse tumor cells in the second part of the program. Fluorescent antibody techniques will be employed to assay development of immunocyte subsets. The results of the low-level exposure study relate directly to the question of inconsistencies between low-dose effects and predictions based on high-dose data. Results of the immunological study will establish the sequence of immunological responses during normal development of the immune system and under conditions of stress induced by environmental pollutants. (1) Carry out joint epidemiological studies to assess effects of changes in the energy levels of neuropsychological processes. (2) Characterize the enhancing and suppressive factors on intracellular effects. (3) Test enhancement of the effect of carcinogens on the immune response. (4) Determine the environmental conditions that increase or depress the energy and activity level of the organism.

MICE

163
Samal, U. C.; Saran, R.; Sanyal, R. K. 1975. **Effects of inhaled fumes on immunological response of rabbits.** *Indian Journal of Physiology and Pharmacology* 19(2):103-104.

RABBITS

164
Sarot, D. A.; Perlmutter, A. 1976. **The toxicity of zinc to the immune response of the zebrafish, Brachydanio rerio, injected with viral and bacterial antigens.** *Transactions American Fisheries Society* 105(3):456-459.

Groups of zebrafish were injected with antigens prepared from infectious pancreatic necrosis virus (IPNV) or Proteus vulgaris. Zn appeared to suppress the immune response against P. vulgaris, but not against IPNV.

Zinc

FISH

165
Savino, A.; Peterson, M. L.; House, D.; Turner, A. G.; Jeffries, H. E.; Baker, R. 1978. **The effect of ozone on human cellular and humoral immunity: characterization of T- and B-lymphocytes by rosette formation.** *Environmental Research* 15(1):65-69.

Healthy male subjects were exposed to 784 g/cu m ozone (O3) for four hr in an exposure chamber; peripheral blood samples were taken and examined for percentages of rosette-forming T-(thymus-derived) and B-(bone marrow-derived) lymphocytes. Blood samples were taken before and after air and O3 exposures and at 72 hr and two weeks following exposure. No statistically

significant depressions in T-lymphocyte rosette formation with sheep erythrocytes were found following exposure to air or O3. However, ability of B-lymphocytes to form rosettes with sensitized human erythrocytes was depressed following ozone exposure. A temporary alteration in surface receptors and/or cell membranes of peripheral blood B-lymphocytes may occur following short-term exposure to O3.

Ozone

HUMAN STUDIES

166
Scheller, S.; Posz, A.; Tustanowski, J.; Ilewicz, L.; Paradowski, Z. 1977. **Certain factors of nonspecific immunity and immunoglobulins in the oral cavity and blood of subjects exposed to chemical stress.** *Czasopismo Stomatologiczne* 30(1):11-16 (POL).

Abnormalities were found in the factors of nonspecific immunity in the serum of subjects occupationally exposed to HCl and H2SO4 vapors. Changes were found in the values of saliva immunoglobulins.

Hydrochloric acid; Sulfuric acid

HUMAN STUDIES

167
Schlueter, D. P.; Banaszak, E. F.; Fink, J. N.; Barboriak, J. 1978. **Occupational asthma due to tetrachlorophthalic anhydride.** *Journal of Occupational Medicine* 20(3):183-188.

Five workers who were involved in the production of epoxy resins developed recurrent respiratory symptoms and physiologic abnormalities following exposure to tetrachlorophthalic anhydride (TCPA). Inhalation challenge with TCPA reproduced the symptoms and demonstrated an immediate and late (four to six hr) physiologic response. Although the clinical picture strongly suggested a hypersensitivity reaction, immunologic studies failed to demonstrate precipitating or specific Ig (immunoglobulin) E antibody. Avoidance of exposure resulted in resolution of symptoms; however, residual functional impairment was seen in three of the five individuals.

Tetrachlorophthalic anhydride; 1,3-Isobenzofurandione, 4,5,6,7-tetrachloro-

HUMAN STUDIES

168
Schnizlein, C. T. 1979. **Effect of acute nitrogen dioxide exposure on lung immunity in the rat.** Paper presented at 12th Annual Meeting of the American Academy of Clinical Toxicology, 11-17 March, New Orleans LA.

Nitrogen dioxide

RATS

169
Schnizlein, C. T.; Bice, D. E. 1980. **Evaluation of immune changes by lung exposure to benzo(a)pyrene and NO2 following intraperitoneal immunization.** *Federation Proceedings* 39(3, Pt. 1):620.

Lung exposure to 26 ppm nitrogen dioxide or 1 mg benzo(a)pyrene (BaP) alters the immune response in the lung-associated lymph nodes (LALN) to antigen instilled into the lung. To determine if the damage causing these changes was in the lung or in the LALN, Fischer-344 rats were immunized with sheep red blood cells intraperitoneally, which allowed antigen to reach the LALN without first being handled by the lung clearance mechanisms. Rats were immunized at various times relative to BaP or nitrogen oxide exposure and the number of antibody-forming cells (AFC) in the LALN and spleen was measured 6 days later. An increased number of antigen-specific IgM and IgG AFC in the LALN was observed when animals were immunized immediately following BaP instillation. There was no difference in the number of AFC in the LALN from control or nitrogen oxide-exposed rats. However, control rats had an increased number of IgM AFC in their spleens compared to nitrogen oxide-exposed rats when animals were immunized one day after exposure. This increase probably represents a response to stress induced by the 24-hr exposure. Our results indicated that the particulate nature of the BaP allowed its trapping by the LALN where it damaged these nodes, whereas the NO2-induced damage was confined to the lung.

Benzo(a)pyrene; Nitrogen oxide

RATS

170
Schuller, G. B.; Kaufman, B. M.; Borzelleca, J. F. 1978. **Effect of four haloalkanes on humoral and cell-mediated immunity in mice.** *Toxicology and Applied Pharmacology* 45(1):329.

The immunological response of ICR mice following administration of chloroform (CHCl3; 0.5, 50, and 150 mg/kg), bromodichloromethane (CHBrCl2; 0.2; 12.5, and 125 mg/kg), bromoform (CHBr3; 0.2, 12.5, and 125 mg/kg), and dibromochloromethane (CHBr2Cl:0.2; 12.5, and 125 mg/kg) by gastric gavage for 90 days was studied. Delayed hypersensitivity (DH) was evaluated by 125I-labeled albumin extravasation into the footpad 18 hr after a second challenge with sheep erythrocytes.

Chloroform; Methane, trichloro-; Dibromochloromethane; Methane, dibromochloro-; Bromoform; Methane, tribromo-

MICE

171
Seinen, W. 1980. **Immunosuppression induced by certain organotin compounds.** *Veterinary Science Communications* 3(4):279-288.

Dibutyltin dichloride; Stannane, dibutyldichloro-; Dioctyltin dichloride; Stannane, dichlorodioctyl-

172
Seinen, W.; Vos, J. G.; VanKrieken, R.; Penninks, A.; Brands, R.; Hooykaas, H. 1977. **Toxicity of organotin compounds. III. Suppression of thymus-dependent immunity in rats by di-n-butyltindichloride and di-n-octyltinchloride.** *Toxicology and Applied Pharmacology* 42(1):213-224.

To evaluate the functional significance of di-n-butyltin dichloride (DBTC)- and di-n-octyltin dichloride (DOTC)-induced lymphoid depletion, various immune function studies were carried out. The delayed-type hypersensitivity reaction was decreased in rats fed 50 or 150 ppm of DOTC for six weeks. This decrease was dose related. Allograft rejection, another cellular immune response, was significantly delayed by DBTC and DOTC. The antibody response against Escherichia coli lipopolysaccharides, probably a T-cell-independent antigen, was not affected by DBTC. However, the humoral immune response against sheep red blood cells (SRBC), requiring cooperation of T-helper-cells and B-cells, was distinctly depressed by DBTC. Hemagglutination and hemolysin titers as well as the number of direct plaque-forming cells against SRBC/spleen were decreased in a dose-related manner by DBTC.

The phagocytic capacity of macrophages of rats was not affected by DOTC as was shown in the C clearance test. Altered immune functions were never found in mice or guinea pigs exposed to DBTC or DOTC. Thus, both DBTC and DOTC induce immune suppression in rats by a selective inhibition of T-lymphocyte activity. Immune suppression was most pronounced in animals exposed during development of the lymphoid system.

Dibutyltin dichloride; Stannane, dibutyldichloro-; Dioctyltin dichloride; Stannane, dichlorodioctyl-

RATS; GUINEA PIGS

173
Sharma, R. P.; Kociba, R. J.; Gehring, P. J. 1978. **Immunotoxicologic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals.** *Toxicology and Applied Pharmacology* 45(1):333.

Male CD-1 mice and White New Zealand rabbits were given 0, 0.01, 0.1, 1, and 10 mg of TCDD/kg/week for up to eight weeks. The mice exhibited lesions primarily in the liver. Thymic changes in mice were pronounced after four weeks, but not after eight weeks. Splenic lymphocytes of both species were cultured in vitro with or without the presence of selective mitogens (phytohemagglutinin and pokeweed mitogen) and the incorporation of (3H)thymidine was measured. Exposure to TCDD, even at the lowest level (0.01 mg of TCDD/kg/week), caused an increase in the thymidine uptake by nonstimulated splenic lymphocytes; the blastogenic response to phytomitogens decreased at higher levels. Additional groups of mice and rabbits were inoculated with an antigenic mixture to evaluate induced immune reactivity. Dose levels of 1 or 10 mg of TCDD/kg/week reduced the serum antitetanus concentrations in both species, and skin reactivity to tuberculin and the antibody producing cells in the popliteal lymph nodes of rabbits. The concentration of serum immunoglobulins was markedly reduced with the higher dose levels of TCDD, but were elevated with the lower dose levels.

TCDD, 2,3,7,8-

RABBITS; MICE

174
Shea, J. W.; Huber, G. L. 1978. **The effect of experimental tobacco smoke inhalation on in vitro alveolar macrophage bactericidal function.** *Journal of Laboratory and Clinical Medicine* 92(2):270-282.

The in vitro antibacterial activity of rat alveolar macrophages against a challenge of radiolabeled Staphylococcus epidermidis was studied following 30 and 60 consecutive days of in vivo tobacco smoke inhalation in a dose equivalent to approximately 1.5 packs of unfiltered cigarettes per day in man. Macrophages, harvested by bronchopulmonary lavage, were cultured, infected, and assayed hourly for three hr to determine the relative percentage of surviving radiolabeled intracellular bacteria. Macrophages harvested from smoke-treated rats for 30 days had an impaired capacity to kill bacteria when compared to macrophages from control and sham-smoked animals. Alveolar macrophages harvested from rats exposed to cigarette smoke for 60 days, however, did not have an impairment in their bactericidal activity relative to matched controls. These data imply that doses of cigarette smoke commonly consumed by man impair the in vitro bactericidal function of the rat alveolar macrophages following 30 consecutive days of experimental smoke treatment. The disappearance of this effect after 60 days of exposure to tobacco smoke suggests an adaptation to the initial impairment.

Tobacco

RATS

175
Shtenberg, A. I.; Ashmenskas, Y. I.; Kusevitskii, I. A. 1972. **Immunobiological body reactivity changes under the effect of some pesticides belonging to the group of carbamine and dithiocarbamine compounds.** *Voprosy Pitaniya* 31(1):58-63.

Agglutinin titers in rats immunized with typhoid vaccine were lowered early in the experiment when multiple oral doses of Sevin, zineb, ziram, and maneb were administered. Complement activity of the blood serum decreased later. Depression of the phagocytic activity of the neutrophiles was observed nine months following treatment with ziram and Sevin. Although phagocytic activity returned to control levels four months following cessation of treatment, agglutinin titers remained at subnormal levels in all treated groups. Complement activity was reduced only in those animals receiving Sevin and ziram. Histochemical and histological investigations of liver and spleen tissue in non-immunized animals revealed a prevalence of dystrophic changes, while immunized rats showed mildly pronounced dystrophic manifestations in cellular elements along with proliferation of hepatic Kupfer's cells, sinusal endothelium, and agglomeration of neutrophil and eosinophil leukocytes in the spleen.

Maneb; Manganese, ((1,2-ethanediylbis(carbamodithioato))(2-))-; Ziram; Zinc, bis(dimethylcarbamodithioato-S,S')-, (T-4)-; Carbaryl; 1-Naphthalenol, methylcarbamate; Zineb; Zinc, ((1,2-ethanediylbis(carbamodithioato))(2-))-

RATS

176
Shtenberg, A. I.; Khovaeva, L. A. 1975. **Immunodepressant action of some pesticides with different conditions of feeding animals.** *Voprosy Pitaniya* 5:61-68 (RUS).

Following long-term chronic administration of increasing doses, pesticides inhibited antibody synthesis. Recovery of ability to form antibodies was delayed, indicating seriously affected immune reactions.

Pesticides

RATS

177
Shubik, V. M.; Nevstrueva, M. A.; Kalnitskii, S. A.; Livshits, R. E.; Merkushev, G. N.; Pilshchik, E. M.; Ponomareva, T. V. 1976. **Effect of chronic enteral administration of radioactive and chemical substances on the immune response.** *Gig. Otsenka Faktorov Radiats. Neradiats. Prir. Ikh Komb.*, pp. 87-91 (RUS).

When ingested with the drinking water for 12 to 24 months, chemicals such as chlorophos, methylmercury, hexamethylenediamine, and BeCl2 were ten times more potent than radionuclides such as 137-Cs, 65-Zn, and 226-Ra in suppressing normal immune indicators, in inducing autoimmune responses, and in disrupting the normal spleen morphology in rats, mice, and rabbits.

Chlorophos; Phosphonic acid, (2,2,2-trichloro-1-hydroxyethyl)-, dimethyl ester; Hexamethylenediamine; 1,6-Hexanediamine; Methylmercury; Beryllium chloride; Zinc; Cesium; Radium

RATS; MICE; RABBITS

178
Shubik, V. M.; Nevstrueva, M. A.; Kalnitskii, S. A.; Livshits, R. E.; Merkushev, G. N.; Pilshchik, E. M.; Ponomareva, T. V. 1978. **Comparative study of changes in immunological reactivity during prolonged introduction of radioactive and chemical substances into the organism with drinking-water.** *Journal of Hygiene Epidemiology Microbiology and Immunology (Prague)* 22(4):408-414.

The effects of radioelements and chemicals in drinking water on immunological parameters in rabbits, rats, and mice were investigated in relation to maximum permissible concentrations and average annual permissible concentrations. Toxic chemicals increased the production of autoantibodies and lowered immunity. Immunological indexes were unchanged after treatment with radionuclide concentrations up to ten-fold the average annual permissible concentration, but at 250-fold the average annual permissible concentration factors of nonspecific immunological protection were inhibited.

Radionuclides

RATS; RABBITS; MICE

179
Silkworth, J. B. 1979. **Modification of cell-mediated immunity by polychlorinated biphenyl (Aroclor 1016) and hexachlorobenzene.** *Dissertation Abstracts International B Sciences and Engineering* 40(10):4735.

Polychlorobiphenyl compounds; Hexachlorobenzene

180
Silkworth, J. B.; Loose, L. D. 1980. **Environmental chemical-induced modification of cell-mediated immune responses.** *Advances in Experimental Medicine and Biology* 121A:499-522.

The effects of environmental chemicals on the host defense mechanism and immune system were investigated. Mice were fed diets containing either 167 ppm Arochlor 1016 (PCB) or 167 ppm hexachlorobenzene (HCB). PCB had no influence on the graft-versus-host activity or the mixed lymphocyte responsiveness of spleen cells isolated from the animals. HCB administration resulted in an approximately 20% suppression of spleen cell activity in the graft-versus-host response, a 44% reduction in mixed lymphocyte cultures, and a 68% reduction of peak control cell response to mitogen stimulation.

Polychlorobiphenyl compounds; Hexachlorobenzene

MICE

181
Silkworth, J. B.; Loose, L. D. 1978. **Cell-mediated immunity in mice fed either Aroclor 1016 or hexachlorobenzene.** *Toxicology and Applied Pharmacology* 45(1):326-327.

A profound impairment of humoral immunity in mice fed 167 ppm PCB 1242 or HCB has been shown in previous studies. A significant reduction in splenic direct antibody plaque-forming cells was observed in the absence of any histopathological alterations in lymphoid tissue. High concentrations of PCB and HCB in primary and secondary lymphoid tissue suggested that the suppression might involve impairment in cellular as well as humoral immunity. To evaluate this possibility, the influence of PCB 1016 and HCB on the donor cells of the graft-versus-host reaction was studied. Male C57B1/6 mice received 167 ppm PCB 1016 or HCB in their diets for three weeks. Spleen cells in three concentrations from these animals were then injected into neonatal BDF1 mice. Spleens from the recipient mice were removed and weighed nine days later and the spleen index calculated. A dose-related response was observed in neonatal BDF1 mice which received the three different concentrations of spleen cells from animals fed control diets. However, the response was not as pronounced in neonates which received spleen cells from PCB-treated mice and even less pronounced in animals which received spleen cells from HCB-treated donor mice. The data indicate an enhancement of cell-mediated immunity, and the disparate dose response may be interpreted to mean that perhaps PCB and HCB may activate in situ donor lymphocytes.

Polychlorobiphenyl compounds; Hexachlorobenzene

MICE

182
Smith, S. H.; Sanders, V. M.; Barrett, B. A. 1978. **Immunotoxicological evaluation on mice exposed to polychlorinated biphenyls.** *Toxicology and Applied Pharmacology* 45(1):330.

PCBs are deleterious to the monocyte macrophage system in ICR neonate and adult mice. Reticuloendothelial system function was measured using 125I-labeled Listera monocytogenes; cell-mediated immunity from sheep red blood cells and footpad swelling from 125I-labeled serum albumin were also measured following acute gavage or s.c. Aroclor 1254 was administered for 14 days to adults (0.3-65 mg/kg) and to neonates (0.3-12.5 mg/kg). Adult mice exhibited a dose-dependent depression of Listera uptake and specific activity (SA). Liver weights increased two-fold at 75 mg/kg s.c. Neonates had no increase in liver size s.c., while only the males had a depression of liver uptake and SA (24%) at 12.5 mg/kg. Adult females exhibited a depression in splenic uptake and SA at 75 mg/kg s.c. Splenic depression was also seen in neonatal males at 0.3 and 12.5 mg/kg s.c. Kidney localization of Listera increased in all exposed mice. Erythrocyte counts were depressed in s.c. mice. Cell-mediated immunity in s.c. adults inhibited 125I-labeled albumin incorporation at 75 mg/kg.

Polychlorobiphenyl compounds

MICE

183
Snella, M. C.; Rylander, R. 1979. **Alteration in local and systemic immune capacity after exposure to bursts of CO.** *Environmental Research* 20(1):74-79.

Immune capacity in the lung, spleen, and pulmonary lymph nodes was studied in adult guinea pigs exposed to carbon monoxide at 5,000 or 10,000 ppm for three min, or 12 times daily for three to four weeks. Seven days prior to termination of exposure the animals were immunized with sheep red blood cells (SRBC). Lower weight increases were noted in all except one exposure group. Also an increased number of pulmonary alveolar macrophages (PAM) was found in all but one group. All groups showed a tendency toward an increase in polymorphonuclear leukocytes (PMN) numbers. Although reductions in numbers of plaque-forming cells were found, these were generally not statistically significant.

Carbon monoxide

GUINEA PIGS

184
Sonntag, A. C. 1975. **Xenobiotics and molecular teratology.** *Clinical Obstetrics and Gynecology* 18(4):199-207.

Disturbances in fetal and perinatal regulatory mechanisms due to exposure to PCBs and DDT are reviewed.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Polychlorobiphenyl compounds

185
Street, J. C.; Sharma, R. P. 1974. **Quantitative aspects of immunosuppression by selected pesticides.** *Toxicology and Applied Pharmacology* 29(1):135-136.

Dose-response evaluations of immune suppression by four insecticides (p,p'-DDT, methyl parathion, carbaryl, and carbofuran) were made following oral administration of these compounds in the diets of rabbits for a 28-day treatment period. On day 29 antigens were injected into the foot pad and the immune status evaluated over the following 28 days of treatment. Using the fluorescent antibody technique, significant suppression was noted with doses as low as 0.92 mg/kg DDT, 0.04 mg/kg methyl parathion, and 0.49 mg/kg carbofuran. Reductions in germinal centers in the spleen as well as thymus cortical atrophy were observed. Although higher doses were required, methyl parathion and DDT apparently suppressed cell-mediated sensitivity to tuberculin. Serum globulin values were not affected, nor were hemagglutinin and hemolysin titers up to 40-fold over those resulting in histological effects. At dosages up to 8.38 mg/kg, carbaryl gave no consistent indications of suppression. This study confirms previous reports of immune suppression by insecticides such as DDT as well as the organophosphate and carbamate compounds studied.

Carbaryl; 1-Naphthalenol, methylcarbamate; Carbofuran; 7-Benzofuranol, 2,3-dihydro-2,2-dimethyl-, methylcarbamate; Methyl parathion; Phosphorothioic acid, O,O-dimethyl O-(4-nitrophenyl) ester; DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

RABBITS

186
Street, J. C.; Sharma, R. P. 1975. **Alteration of induced cellular and humoral immune responses by pesticides and chemicals of environmental concern: quantitative studies of immunosuppression by DDT, Aroclor 1254, carbaryl, carbofuran, and methylparathion.** *Toxicology and Applied Pharmacology* 32(3):587-602.

Dietary treatment of rabbits with DDT (0.184 to 6.54 mg/kg/day), Aroclor 1254 (0.18 to 6.54 mg/kg/day), carbaryl (0.23 to 8.38 mg/kg/day), carbofuran (0.03 to 1.05 mg/kg/day), and methyl parathion (0.036 to 1.479 mg/kg/day), for four weeks followed by a challenge with sheep red blood cells and Freund's adjuvant resulted in a decreased plasma count in popliteal nodes (except with carbaryl), reduction of germinal centers in the spleen, and increased thymus cortex atrophy. The antigen-induced increase in serum gamma-globulin was consistently decreased with DDT, Aroclor, carbaryl, and carbofuran treatments, but only carbaryl produced significant changes (at ten days postantigen). DDT-treated groups showed significantly higher preantigen gamma-globulin values which were less evident following antigen challenge. Skin sensitivity to tuberculin was decreased (except with carbaryl) but generally only at higher dosages. None of the compounds showed any effect on growth; food consumption; leukocyte count; or on organ-to-body-weight ratios for liver, kidney, spleen, and adrenal, except for slight liver enlargement caused by Aroclor 1254.

Carbaryl; 1-Naphthalenol, methylcarbamate; Carbofuran; 7-Benzofuranol, 2,3-dihydro-2,2-dimethyl-, methylcarbamate; Methyl parathion; Phosphorothioic acid, O,O-dimethyl O-(4-nitrophenyl) ester; DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

RABBITS

187
Thigpen, J. E.; Faith, R. E.; McConnell, E. E.; Moore, J. A. 1975. **Increased susceptibility to bacterial infection as a sequela of exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin.** *Infection and Immunity* 12(6):1319-1324.

Effects of subclinical levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on the response of mice to infection with Salmonella bern or Herpesvirus suis (pseudorabies virus) are reported. TCDD, a contaminant of certain commercially useful chemicals, causes thymic atrophy and suppresses cell-mediated immunity in laboratory animals. Sublethal levels of TCDD were given through a gastric tube once weekly for four weeks. Dosages of 1 micro-g or more, followed by Salmonella infection, resulted in significant increases in mortality and decreases in the time from infection to death. TCDD showed no significant effect on mortality in pseudorabies-infected mice. Extremely low levels of TCDD, which do not result in pathological or clinical change, have the capacity to affect host-defense mechanisms.

TCDD, 2,3,7,8-

MICE

188
Thomas, G. B.; Fenters, J. D.; Ehrlich, R. 1979. **Effect of exposure to PAN and ozone on susceptibility to chronic bacterial infection.** *U.S. NTIS Report* PB-292267, 44 pp.

The effects of peroxyacetyl nitrate (PAN) and ozone (O3) on susceptibility of mice and guinea pigs to chronic and acute respiratory infections were studied. Streptococcus sp. was used for the acute infectious disease and Mycobacterium tuberculosis served as the agent for chronic respiratory infection. A significant increase in mortality due to streptococcal pneumonia was seen upon a single three hr exposure to PAN in concentrations ranging from 14.8 to 28.4 mg/cu m. Multiple daily exposures to 4.9 or 7.4 mg/cu m PAN three hr/day, five days/week for up to three weeks had no effect on mortality, survival rates, or ability to clear inhaled Streptococcus sp. from the lungs. Daily three hr exposures to 25.0 mg/cu m PAN did not produce any marked changes in the chronic infection as measured by M. tuberculosis titers in the lungs. The diameter of erythemas, expressing the cutaneous delayed hypersensitivity reaction, were persistently smaller in guinea pigs exposed to PAN. Multiple exposures to 19.8 mg/cu m PAN resulted in initial elevation of antibody titers, but depression of titers during the later (12 to 15 weeks) observation period. A single exposure to the same concentration of PAN resulted in a significant increase in total number of cells lavaged from their lungs but somewhat decreased levels of adenosine triphosphate. Exposure to 7.4 mg/cu m PAN three hr/day, five days/week for two weeks resulted in reduced total cell counts and a significant reduction of ATP levels in alveolar macrophages.

Peroxyacetyl nitrate; Ozone

MICE; GUINEA PIGS

189
Thomas, P. T.; Hinsdill, R. D. 1978. **Effect of polychlorinated biphenyls on the immune responses of rhesus monkeys and mice.** *Toxicology and Applied Pharmacology* 44(1):41-51.

Female rhesus monkeys were fed either normal chow or chow containing 2.5 or 5.0 ppm of Aroclor 1248 (PCB). After six months, the PCB-fed monkeys developed chloracne, alopecia, and facial edema. After 11 months, control and treated monkeys were immunized with sheep red blood cells (SRBCs) and tetanus toxoid (TT). Monkeys fed 5.0 ppm of PCB had significantly lower anti-SRBC antibody titers than controls at only two intervals following primary immunization. Antibody response to TT was not measurably affected by PCB exposure. Both PCB-fed groups

had consistently lower gamma-globulin levels than controls. These results indicate that sustained exposure to low levels of PCB could have modest to slight immunosuppressive effects, which might be important depending on the general health of the individual. Mice fed up to 1000 ppm of PCB for three to five weeks exhibited no signs of PCB intoxication other than liver hypertropy. However, these mice, when challenged with Salmonella typhimurium, showed higher mortality and significantly greater numbers of viable organisms in the spleen, liver, and blood than did controls. Similarly, exposed mice showed an increased sensitivity to endotoxin. Thus, mice exposed to subclinical doses of PCB appear to have an impaired ability to withstand challenge by pathogens and an increased sensitivity to endotoxin.

Polychlorobiphenyl compounds

MONKEYS; MICE

190
Thomas, R. T.; Hinsdill, R. D. 1979. **The effect of perinatal exposure to tetrachlorodibenzo-p-dioxin on the immune response of young mice.** *Drug and Chemical Toxicology* 2(1/2):77-98.

Immunocompetence in offspring of female mice fed 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) was investigated. A significant dose-related decrease in plaque-forming cells was noted in the offspring of mothers fed 5 ppb TCDD. In addition, sensitivity to dinitrofluorobenzene was significantly reduced in mice from mothers fed 5 ppb. No significant differences from controls in in vitro blastogenic response of splenic T- and B-cells to E. coli lipopolysaccharide and concanavalin A was noted from controls. Offspring whose mothers were treated with up to 5 ppb TCDD showed no difference in percent mortality from controls. A marked increase in Salmonella endotoxin sensitivity directly proportional to TCDD exposure was noted in offspring whose mothers were fed as little as 1 ppb TCDD. No significant differences in differential white cell counts between offspring from control mice or mice fed up to 5 ppb of TCDD were noted.

TCDD, 2,3,7,8-

MICE

191
Thurman, G. R.; Simms, B. G.; Goldstein, A. L.; Kilian, D. J. 1978. **The effects of organic compounds used in the manufacture of plastics on the responsivity of murine and human lymphocytes.** *Toxicology and Applied Pharmacology* 44(3):617-641.

The immunological response to benzene; 1,4-dioxane (dioxane); toluene diisocyanate (TDI); vinyl chloride; vinylidene chloride; ethyleneimine; and epichlorohydrin was measured in vitro with human and murine lymphocytes and in vivo in mice. Immunological activators were used as controls. Dioxane suppressed T-cell responses in mouse lymphocytes in vitro, while increasing B-cell responses; human lymphocytes were unaffected. In vivo, 0.5 ml daily injections of 20% dioxane were fatal to CBA/J mice. TDI stimulated human and murine lymphocytes and mouse spleen cells in vivo at several concentrations. Vinylidene chloride was the least toxic to lymphocytes of all compounds studied. Ethylenimine inhibited human lymphocytes greater than those of mice; in vivo, it altered the spleen response to plant lectin, phytohemagglutinin. Epichlorohydrin is toxic to both human and murine lymphocytes, especially those which have not fully matured.

Benzene; Toluene diisocyanate; Benzene, 1,3-diisocyanatomethyl-; Vinyl chloride; Ethene, chloro-; Vinylidene chloride; Ethene, 1,1-dichloro-; 1,4-Dioxane; Ethyleneimine; Aziridine; Epichlorohydrin; Oxirane, (chloromethyl)-

MICE

192
Tripp, M. R. **Pollutant responses in marine animals (PRIMA) - histopathology and immunity as indicators of chemical stress.** Research at University of Delaware, Department of Biological Sciences, Lewes DE; Sponsored by NSF, Washington DC, code OCE77-24037; 3/78-8/79.

PRIMA is a closely coordinated, multi-disciplinary field and laboratory study to develop and evaluate biological indices of impending organic pollutant damage to marine animals. It will focus on the effects of selected aromatic hydrocarbons (benzo(a)pyrene, benz(a)anthracene, fluoranthene) and related halogenated compounds (hexachlorobenzene, pentachlorophenol) on certain biochemical and morphological changes in representative marine organisms. Attention will be given to the: accumulation of test chemicals in tissues of exposed animals, changes in metabolic products associated with stress reactions, changes in activity of biotransforming enzymes, changes in cell and tissue structure, and changes in immune competence. This award funds the measurement of histopathological changes in marine animals by examining selected tissues under the light and electron microscope. Special emphasis will be placed on respiratory, digestive, and reproductive tissues. Immune responses in fish will be determined by measuring cellular immunity by scale transplantation and humoral immunity by antibody formation. The results of these studies will be correlated with biochemical and physiological parameters to make some generalizations about reactions of benthic invertebrates and fish to selected classes of organic compounds.

Benzo(a)pyrene; Benz(a)anthracene; Fluoranthene; Hexachlorobenzene; Pentachlorophenol

FISH

193
University of California, Irvine. 1980. **Proceedings of the Conference on Environmental Toxicology (10th) held in Dayton, Ohio, on 13, 14, and 15 November 1979.** *U.S. NTIS Report* AD-A086341, 292 pp.

Major technical areas discussed included environmental hazards of fibrous dusts, toxicokinetics of inhaled gases and vapors, and the environmental hazards of toxicants in surface water systems. The oncogenic effects of hydrazine in animal models and immunotoxic reactions as manifested by skin and lung hypersensitivity were presented.

Hydrazine

194
Vasileva, E. V.; Ermakova, N. G.; Orlova, A. A. 1977. **Specific humoral and cellular responses in berylliosis.** *Gigiena Truda i Professional'nye Zabolevaniya* 7:8-12 (RUS).

The study was made on healthy individuals occupationally dealing with Be and in patients suffering from berylliosis. In reactions of passive hemagglutination with sheep erythrocytes sensitized with BeCl2 solution, the antiberyllium factor was present in 49% of the healthy subjects and in 59-75% of the patients suffering from berylliosis. The highest level of antiberyllium antibodies was recorded in persons with an interstitial form of berylliosis. The cellular sensitization with respect to Be was determined by skin drop tests with a BeSO4 solution. Both tests, though failing to show a complete correlation, disclosed the maximum sensitization with respect to Be in patients with an active stage of granulomatous form of berylliosis.

Beryllium

HUMAN STUDIES

195
Vijay, H M.; Mendoza, C. E.; Lavergne, G. 1978. **Production of homocytotropic antibodies (IgE) to malathion in the rat.** *Toxicology and Applied Pharmacology* 44(1):137-142.

Outbred and inbred Wistar rats were immunized with a single i.p. injection of a mixture of a conjugate of malathion residue-bovine serum albumin and aluminum hydroxide gel. Eleven days after immunization, reaginic antibodies (IgE) specific to malathion residue were detected by a 48 hr passive cutaneous anaphylaxis reaction (PCAR) using malathion residue-rabbit c-globulin conjungate. Maximum response of these antibodies was observed on day 18 postimmunization. Antisera heated at 56 degrees C for four hr failed to elicit a four-hr PCAR against malathion residue-RbcG, indicating a lack of IgGa antibody to malathion residue. The inbred rats seemed to respond better than the outbred rats.

Malathion; Butanedioic acid, ((dimethoxyphosphinothioyl)thio)-, diethyl ester

RATS

196
Vos, J. G.; DeRoij, T. 1972. **Immunosuppressive activity of a polychlorinated biphenyl preparation on the humoral immune response in guinea pigs.** *Toxicology and Applied Pharmacology* 21(4):549-555.

The number of gamma-globulin-containing cells in popliteal lymph nodes was significantly reduced in guinea pigs fed Aroclor 1260 (0, 10, and 50 ppm in the diet for eight weeks) and injected with tetanus toxoid to stimulate the lymphoid system. There was also a significant reduction of gamma-globulin levels in the serum of toxoid-stimulated animals fed 10 ppm Aroclor 1260. These facts indicate that some immunosuppression is produced by feeding Aroclor 1260. This study demonstrates the danger of immunosuppression by this widespread pollutant even at low feeding levels.

Polychlorobiphenyl compounds

GUINEA PIGS

197
Vos, J. G.; Kreeftenberg, J. G.; Engel, H. W. B.; Minderhoud, A.; VanNoorle-Jansen, L. M. 1978. **Studies on 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced immune suppression and decreased resistance to infection: endotoxin hypersensitivity, serum zinc concentrations and effect of thymosin treatment.** *Toxicology* 9(1/2):75-86 (RUS).

Sublethal doses of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) caused thymus atrophy in several species and induced suppression of cell-mediated immunity as measured by different parameters. The selective effect on thymus was not likely caused by a cytotoxic effect on lymphocytes or by an effect on pituitary or adrenals. Mice received daily injections with thymosin in order to study whether reduced production of thymic hormones could be involved in the atrophy. Also, serum Zn concentrations were measured. As thymosin injections did not increase thymus weight and mitogenic responsiveness of thymocytes, and Zn levels were not depressed, the mode of action of TCDD-induced thymus atrophy remains unknown. TCDD markedly decreased resistance of mice to infection with Salmonella bern; the increased susceptibility was likely due to the endotoxin content of the bacteria: pretreatment of mice with single or repeated doses of TCDD markedly enhanced their susceptibility to endotoxin even at dose levels that did not produce thymus atrophy. TCDD did not impair nonspecific killing and phagocytosis of Listeria monocytogenes or macrophage reduction of nitro-blue tetrazolium. The immunosuppression was probably only due to an effect on T-lymphocytes and not due to a combined effect on both T-cells and macrophages. The endotoxin hypersensitivity was not the result of alteration in phagocytic function of macrophages.

TCDD, 2,3,7,8-

MICE

198
Vos, J. G.; Kreeftenberg, J. G.; Kater, L. 1978. **Immune suppression by TCDD.** *Monographs of the Giovanni Lorenzini Foundation* 1 (Dioxin: Toxicol. Chem. Aspects):163-175.

Daily subcutaneous thymosin injections caused decreased body weight but no alteration in thymus weight of 22 day-old 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-treated mice. Pretreatment of mice with TCDD enhanced their susceptibility to Escherichia coli endotoxin. Apparently, TCDD-induced lymphocyte depletion in the thymus was not through a reduced production of thymic hormones. The sensitivity effect of TCDD for endotoxin offers a logical explanation for the decreased resistance of TCDD-exposed mice to bacterial infection.

TCDD, 2,3,7,8-

MICE

199
Vos, J. G.; VanGenderen, H. 1973. **Toxicological aspects of immunosuppression.** *Pestic. Environ.: Continuing Controversy, Pap. Inter-Am. Conf. Toxicol. Occup. Med., 8th,* ed. W. B. Deichmann, pp. 527-545. New York: Stratton.

A review with 33 references.

200
Vos, J. G.; VanLogten, M. J.; Kreeftenberg, J. G.; Kruizinga, W. 1979. **Hexachlorobenzene-induced stimulation of the humoral immune response in rats.** *Annals of the New York Academy of Sciences* 320:535-550.

Humoral immunity, cell-mediated immunity, and the phagocytizing capacity of macrophages were studied in rats fed hexachlorobenzene. The humoral response was stimulated as was the in vitro response of spleen cells to different mitogens, but cell-mediated immunity was unaffected. These findings were in disagreement with data from the literature. Susceptibility to endotoxin was increased marginally. An insignificant depression was noted in the phagocytic index.

Hexachlorobenzene

RATS

201
Vos, J. G.; VanLogten, M. J.; Kreeftenberg, J. G.; Steerenberg, P. A.; Kruizinga, W. 1979. **Effect of hexachlorobenzene on the immune system of rats following combined prenatal and postnatal exposure.** *Drug and Chemical Toxicology* 2(1/2):61-76.

The effect of HCB on the immune system of rats was studied after combined pre- and postnatal exposure. Cell-mediated immunity was slightly suppressed. Results from assays for humoral immune function including antibody response to tetanus toxoid, to T. spiralis, to LPS, and responsiveness of spleen cells to the B-cell mitogen LPS showed that humoral immunity is strongly

enhanced in animals treated pre- and postnatally with HCB. The developing immune system seems particularly susceptible to HCB.

Hexachlorobenzene

RATS

202
Wagner, V.; Andrlikova, J.; Palek, V.; Wagnerova, M. 1978. **The levels of immunoglobulins (IgG, IgA, IgM) under the effect of age and exposure to the mining environment in uranium industry.** *Strahlentherapie (West Germany)* 154(6):406-412.

IgG, IgA, and IgM levels were measured in 347 miners working in underground U mines, in 156 men beginning mine work, and 101 men working in the food industry, all in central Bohemia. Significantly elevated IgG and IgM levels were found in miners exposed less than 5 years and elevated IgA levels in the group exposed for more than 15 years. IgG levels decline significantly in miners older than 31 years.

Uranium

HUMAN STUDIES

203
Ward, A. M.; Udnoon, S.; Watkins, J.; Walker, A. E.; Darke, C. S. 1976. **Immunological mechanisms in the pathogenesis of vinyl chloride.** *British Medical Journal* 1:936-938.

Results from immunological investigations performed on 58 workers from a vinyl chloride polymerization plant are presented. Pathogenic mechanisms of vinyl chloride disease are explained and some conclusions drawn about its etiology. Immunological and immunochemical investigations showed the presence of circulating immune complexes in 19 of 28 patients with the disease and in 2 of 30 workers exposed to vinyl chloride. The results suggest that this disease is an immune complex disorder and that the immune response is initiated by the adsorption of vinyl chloride or a metabolite to tissue or plasma protein.

Vinyl chloride; Ethene, chloro-

HUMAN STUDIES

204
Wassermann, M.; Wassermann, D. 1971. **Effects of organochlorine insecticides on homeostatic and immunologic processes.** *International IUPAC Congress of Pesticide Chemistry* 6:521-529.

Pesticides

205
Wassermann, M.; Wassermann, D.; Gershon, Z.; Zellermayer, L. 1969. **Effects of organochlorine insecticides on body defense systems.** *Annals of the New York Academy of Sciences* 160(1):393-401.

Pesticides

206
Wassermann, M.; Wassermann, D.; Kedar, E.; Djavaherian, M. 1971. **Immunological and detoxication interaction in p,p'-DDT fed rabbits.** *Bulletin of Environmental Contamination and Toxicology* 6(5):426-435.

DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-

RABBITS

207
Wilde, K.; Chang, Y. F.; Joseph, J. M. 1974. **Effect of chronic exposure to low levels of heavy metals on the immune mechanisms in the guinea pig.** *Abstracts of the Annual Meeting of the American Society for Microbiology* 74:134.

Metals

GUINEA PIGS

208
Wilde, K.; Chang, Y. F.; Joseph, J. M. 1977. **The effect of chronic exposure to low levels of environmental metals on immune mechanisms.** *Abstracts of the Annual Meeting of the American Society for Microbiology* 77:111.

Metals

209
Wiltrout, R. W.; Ercegovich, C. D.; Ceglowski, W. S. 1978. **Humoral immunity in mice following oral administration of selected pesticides.** *Bulletin of Environmental Contamination and Toxicology* 20(3):423-431.

Effects of representatives of several widely used pesticide classes (carbaryl, DDT, parathion, chlordimeform, ametryne) on the primary immune response of experimental animals were investigated. All of the pesticides tested were observed to induce statistically significant suppression of the humoral immune response if administered orally at near lethal doses, during an ongoing immune response. Chlordimeform and ametryne were also observed to have a suppressive effect on humoral immune competence if given orally in a sufficiently large quantity at the time of or prior to immunization.

Ametryne; 1,3,5-Triazine-2,4-diamine, N-ethyl-N'-(1-methylethyl)-6-(methylthio)-; Carbaryl; 1-Naphthalenol, methylcarbamate; Chlordimeform; Methanimidamide, N'-(4-chloro-2-methylphenyl)-N,N-dimethyl-; DDT; Benzene, 1,1'-(2,2,2-trichloroethylidene)bis(4-chloro-; Parathion; Phosphorothioic acid, O,O-diethyl O-(4-nitrophenyl) ester

MICE

210
Zarkower, A. 1972. **Alterations in antibody response induced by chronic inhalation of sulfur dioxide and carbon.** *Archives of Environmental Health* 25(1):45-50.

Chronic exposure to carbon or sulfur dioxide, alone or in combination, induced immunosuppressive effects in mice. A reduction in antibody formation to Escherichia coli antigen (aerosol form) occurred in mice exposed to 2.0 ppm SO2 for 192 days. An enhancement of antibody production occurred in the mediastinal lymph nodes after 102 and 135 days of exposure, but this effect was reversed at 192 days. An enhancement of antibody production was observed in spleens of mice exposed to SO2 alone for 135 days. This adjuvant activity decreased by 192 days of exposure, although not to the degree observed in animals exposed to carbon alone.

Carbon; Sulfur dioxide

MICE

211
Zarkower, A.; Scheuchenzuber, W. J.; Burns, C. A. 1979. **Effects of silica dust inhalation on the susceptibility of mice to influenza infection.** *Archives of Environmental Health* 34(5):372-376.

Mice were exposed to silica dust for periods up to six weeks. The ability of the splenic lymphocytes to respond to T- and B-cell mitogens was determined. Resistance to influenza virus infections was tested after three and 20 weeks of exposure. Depressed response to T-cell mitogens was noted at 21 and 27 weeks of silica exposure, but there was no effect on the T-cell responses after 15, 33, and 36 weeks or on B-cell responses after all exposure times. No changes could be detected in the ability of the mice to resist pulmonary influenza virus infections or in the survivors' ability to form hemagglutination-inhibition antibodies against this virus.

Silica

MICE

212
Zeiss, C. R.; Patterson, R.; Pruzansky, J. J.; Miller, M. M.; Rosenberg, M.; Levitz, D. 1977. **Trimellitic anhydride-induced airway syndromes: clinical and immunologic studies.** *Journal of Allergy and Clinical Immunology* 60(2):96-103.

A description is given of a spectrum of respiratory symptoms in workers exposed to trimellitic anhydride (TMA), a biologically active chemical used in the plastics industry. Respiratory syndromes induced by TMA inhalation included asthma and rhinitis of the immediate type, late onset asthma with systemic symptoms, and airway irritation. TMA couples rapidly to human serum albumin, forming an immunoreactive hapten-protein complex. The workers' immunological reactivity to this complex could be quantitated and correlated with the three respiratory syndromes.

Trimellitic anhydride; 5-Isobenzofurancarboxylic acid, 1,3-dihydro-1,3-dioxo-

HUMAN STUDIES

213
Zhigunov, N. F. 1975. **Techniques for studying industrial environmental factors on the heterogeneity of O- and Vi-antibodies.** *Gigiena i Sanitariya* (11):76-79 (RUS).

The immune response of workers making viscose and of others making Lavsan to repeated inoculations with typhoid antigen was determined. The antibodies were differentiated into cysteine-stable (7 S) and cysteine-sensitive (19 S) by the method of E. V. Chernokhvostova (1965). This is believed to make some responses visible that do not appear in the usual serological test. There were marked and more rapid increases in 7 S antibodies in workers exposed to less healthy conditions; H2S and CS2 in one case and dimethyl terephthalate and MeOH in the other.

Carbon disulfide; Lavsan; Poly(oxy-1,2-ethanediyloxycarbonyl-1,4-phenylenecarbonyl); Hydrogen sulfide; Methanol; Dimethyl terephthalate; 1,4-Benzenedicarboxylic acid, dimethyl ester; Rayon

HUMAN STUDIES

214
Ziprin, R. L.; Fowler, S. R. 1977. **Rosette-forming ability of alveolar macrophages from rat lung. Inhibition by hexachlorobenzene.** *Toxicology and Applied Pharmacology* 39(1):105-109.

Adult male rats were fed diets containing 250 ppm hexachlorobenzene. They were maintained on this diet for eight to ten weeks, at which time they were killed and alveolar macrophages were washed from their lungs. The antibody-binding ability (Fc receptor activity) of these cells was measured by quantitating the percentage of rosette formation at fixed antibody concentration. Rosette formation by cells recovered from hexachlorobenzene-treated rats was distinctly lower than that from untreated rats.

Hexachlorobenzene

RATS

215
Zukoski, C. F. **Effects of zinc on lymphocyte function.** Research at U.S. Veterans Administration, Department of Medicine and Surgery Medical Center, Tucson AZ; Sponsored by Veterans Administration, Washington DC, code 423-28-5682, 678-004-P; 3/77-N/A.

Further progress toward understanding the relationship between zinc and immune system function has been made. (1) Zinc and athymic "nude" mice: Tissue zinc levels in immune-deficient nude mice were compared to their normal heterozygous litter mates (N equals 99) at different ages. Large, statistically significant differences were consistently found to occur with nude animals having much higher tissue zinc levels. The data suggest a nude gene-linked difference in post-natal zinc metabolism and represent the first such report in the literature. This finding is of particular interest in view of work demonstrating that high in vivo zinc levels inhibit several immune functions. (2) Plasma membrane zinc: Earlier studies on the role of intrinsic membrane zinc in cell function have been extended. The major portion of erythrocyte ghost zinc is linked to a high molecular weight (100,000 Dalton) intrinsic membrane protein. Remaining membrane zinc was primarily associated with phospholipids. (3) Work recently initiated: An in vivo method has been developed in sheep to study a single lymph node (popliteal) response to injected allogenic cells or implanted renal tissue. This model permits longitudinal study of a developing immune response in terms of both humoral and cell-mediated processes and will be used to investigate the effects of zinc and other immunosuppressives in vivo. Methods are also being developed to study the effects of zinc on lymphocyte microtubule and microfilament function.

Zinc

SHEEP; MICE

CHEMICAL NAME INDEX

SPECIES INDEX

TITLE INDEX

TOXICOLOGY INFORMATION RESPONSE CENTER
INFORMATION CENTER COMPLEX

TOXICOLOGY INFORMATION PROGRAM

The Toxicology Information Response Center (TIRC) was founded in 1971 to establish a national and international center for toxicology information. TIRC provides information to all individuals on a variety of chemicals such as food additives, pharmaceuticals, industrial chemicals, environmental pollutants, heavy metals, and pesticides; and other topics of toxicologic concern.

ORGANIZATION—TIRC is sponsored by the National Library of Medicine's Toxicology Information Program. Located at the Oak Ridge National Laboratory, TIRC is part of the Information Center Complex, a major scientific and technical unit within the Information Division. This Complex coordinates the functions and activities of several information units at the Laboratory. These associations provide a unique opportunity for scientific and technical interactions.

INFORMATION SERVICES—As an information analysis center, TIRC acquires, selects, stores, retrieves, evaluates, analyzes, and synthesizes comprehensive literature packages according to a user's specific request or a current need. TIRC provides extensive toxicology information assistance and reference services to the scientific, administrative, and public communities—health science students, educators, practitioners, scientists, and administrators. Interested persons may request: (1) specific published toxicology data, (2) individualized literature searches, (3) topical bibliographies, (4) annotated and/or key-worded bibliographies, (5) state-of-the-art overviews, (6) custom searches of computerized data bases, (7) SDI service, (8) access to over 650 bibliographic collections generated annually, (9) in-Center use of the toxicology reference library, and (10) selected reports available from the National Technical Information Service.

INFORMATION RESOURCES—TIRC utilizes a variety of information sources. On-line access is available to several computerized data systems: MEDLINE and TOXLINE, RECON, and the diversified files of commercially available data systems such as DIALOG® (Lockheed), ORBIT® (Systems Development Corporation), and BRS® (Bibliographic Retrieval Services, Inc.). The ORNL data files are searchable in batch mode and also provide SDI service.

Hard copy secondary sources used by TIRC include *Biological Abstracts, BioResearch Index, Chemical Abstracts, Current Contents, Excerpta Medica, Index Medicus, ATOMINDEX, Science Citation Index, Energy Research Abstracts, Nutrition Abstracts and Reviews, Air Pollution Abstracts,* and others. In addition, the ORNL library system provides an abundance of valuable resources with more than 250,000 bound volumes and 800,000 technical reports. Of the 4,000 subscription journals, about 1,200 are biologically or environmentally oriented.

As part of the Information Center Complex, TIRC maintains ready access to consultation and information exchange with other distinct, discipline-oriented entities which specialize in: (1) preparing evaluative multimedia monographs, state-of-the-art reviews and overviews, (2) building an interactive computerized Toxicology Data Bank, (3) constructing and maintaining computerized reference and data files on mutagens and teratogens, (4) compiling environmentally oriented data files, and (5) collecting and distributing published energy information as well as ongoing research and development data.

SEARCH REQUEST INFORMATION—Literature searches are initiated after receiving from the requester certain background information: (1) definition of the search request in detail, (2) subject, scope, time and literature coverage, languages, suggested completion date, and (3) agreement on the cost estimate of the completed search.

COST—Searches are accomplished for requesters under a fee-for-services system. The rate is $30/hour with a minimum charge of $35 for domestic search requests. Charges for search requests from foreign countries are $35/hour with a $40 minimum charge. Computer-associated charges, reproduction costs, as well as use fees for copyrighted materials, are assessed in addition to the hourly rate.

Following agreement between TIRC and the requester, a thorough literature search is conducted utilizing on-line computerized data bases and traditional library sources. Scope, time coverage, and search parameters determine the overall search cost.

Payment is collected by the National Technical Information Service in Springfield, Virginia 22161, either by direct billing or through deposit accounts.

Work for government agencies can be accomplished through interagency agreements.

SEARCH COMPLETION TIME—Response times vary from an immediate telephone answer to eight to twelve days for computerized data base searching to three to four weeks for detailed literature searches.

PERSONNEL—TIRC's professional staff members possess multidisciplinary scientific backgrounds covering chemistry, biology and medicine, pharmacology and toxicology, microbiology, bacterial physiology, information sciences, and administration. The staff specializes in bibliographic literature compilations, state-of-the-art overviews, and consultations. Scientific interaction occurs with personnel from the other information centers within the Information Center Complex as well as with the multidisciplinary Laboratory research staff.

CONTACT THE CENTER—Telephone inquiries can be made by direct dialing (615)576-1743. For those who have access to the Federal Telecommunications System (FTS), the number is 626-1743. Written requests for information or searches should be mailed to:

Toxicology Information Response Center
Oak Ridge National Laboratory
Post Office Box X, Building 2024
Oak Ridge, Tennessee 37830

TIRC PUBLICATIONS

ORNL/TIRC-76/2*
Trichloroethylene: I. An Impact Overview. E. M. Waters, H. B. Gerstner, and J. E. Huff. II. An Abstracted Literature Collection, 1907-1976. E. M. Waters and S. A. Black. 265 pages, 1,673 references, $20.00.

ORNL/TIRC-76/3*
Kepone. I. A Literature Summary. J. E. Huff and H. B. Gerstner. II. An Abstracted Literature Collection, 1952-1977. S. A. Black. 52 pages, 175 references, $15.00.

ORNL/TIRC-76/4*
Mirex. I. An Overview. E. M. Waters. II. An Abstracted Literature Collection, 1947-1976. E. M. Waters. 98 pages, 325 references, $10.00.

ORNL/TIRC-76/6*
Lead Analysis: Literature Collection, 1966-1976. S. A. Black and K. C. Miller. 214 pages, 1,552 references, $18.00.

ORNL/TIRC-77/1*
Selected Case Histories and Epidemiological Examples of Human Mercury Poisoning. I. State-of-the-Art Review. Herbert B. Gerstner and J. E. Huff. II. An Abstracted Literature Collection, 1947-1976. S. A. Black. 101 pages, 566 references, $20.00.

ORNL/TIRC-77/2*
Methoxyflurane. I. An Overview. E. M. Waters and B. E. Ricci. II. An Abstracted Literature Collection, 1947-1976. B. E. Ricci and E. M. Waters. 120 pages, 1,071 references, $22.50.

ORNL/TIRC-77/3*
Vinylidene Chloride. I. An Overview. II. A Literature Collection, 1947 to 1977. H. S. Warren and B. E. Ricci. 52 pages, 117 references, $15.00.

ORNL/TIRC-77/4*
Health Aspects of Chloroform—A Review. S. G. Winslow and H. B. Gerstner. An Abstracted Literature Collection, 1907 to 1977. S. G. Winslow. 252 pages, 1,387 references, $28.00.

ORNL/TIRC-77/5*
Asbestos: A Perspective. I. An Overview. J. E. Huff. II. An Annotated Literature Collection, 1960-1974. J. E. Huff, A. S. Hammons, C. Y. Dinger, B. W. Kline, and B. L. Whitfield. III. An Abstracted Literature Compilation, 1974-1977. S. A. Black. 214 pages, 867 references, $28.00.

ORNL/TIRC-78/2*
Polychlorinated Biphenyls, Polybrominated Biphenyls, and Their Contaminants: Literature Compilation, 1965-1977. S. G. Winslow and H. B. Gerstner. 374 pages, 2,068 references, $25.00.

ORNL/TIRC-78/3*
Vinyl Chloride. A Review, 1835-1975. An Annotated Literature Collection, 1835-1975. A Literature Compilation, 1976-1977. H. S. Warren, J. E. Huff, and H. B. Gerstner. 218 pages, 1,153 references, $28.00.

ORNL/TIRC-78/4*
Leptophos. An Overview. A Literature Compilation, 1969-1979. E. M. Waters and Herbert B. Gerstner. 94 pages, 501 references, $17.50.

ORNL/TIRC-78/5*
Health and Environmental Effects of Toxaphene — A Literature Compilation, 1962-1978. S. A. Mashburn. 114 pages, 853 references, $17.50.

NLM/TIRC-80/1**
Health and Environmental Effects of Acid Rain. An Abstracted Literature Collection, 1966-1979. N. S. Dailey and S. G. Winslow. 202 pages, 961 references, $15.00.

NLM/TIRC-80/2**
Asbestos in Air. A Bibliography with Abstracts, 1964-1980. J. G. Pruett and S. G. Winslow. 60 pages, 173 references, $7.00.

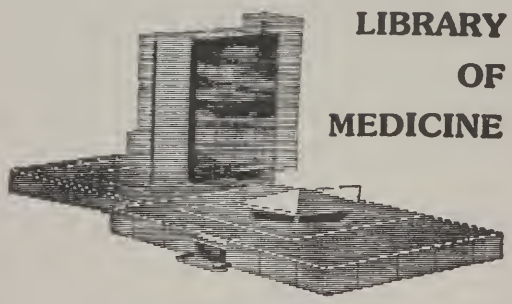
NLM/TIRC-80/3**
Chemical Waste Disposal — Chemicals Identified in Terrestrial and Aquatic Waste Disposal Processes. A Selected Bibliography with Abstracts, 1964-1979. J. G. Pruett and S. G. Winslow. 82 pages, 150 references, $10.00.

NLM/TIRC-80/4**
Health Aspects of Urea-Formaldehyde Compounds. A Selected Bibliography with Abstracts, 1964-1980. N. P. Drago, J. G. Pruett, and S. G. Winslow. 52 pages, 122 references, $7.50.

NLM/TIRC-81/1**
Toxicity of Selected Vanadium Compounds. A Bibliography with Abstracts, 1965-1980. N. S. Dailey, S. A. Mashburn, and S. G. Winslow. 100 pages, 261 references $15.00.

*Available from the National Technical Information Service, Springfield, Virginia 22161.

**Available from the Federation of American Societies for Experimental Biology, Bethesda, Maryland 20014.



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